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Anjana Perianayagam, Stephen Silver, Ruth Kouides, Richard Sterns. Rochester General Hospital, Rochester, New York, USA

29 Beer Potomania: A Unique Cause of Hyponatremia at High Risk of Complications from Rapid Correction
Shalin R. Sanghvi, Paul S. Kellerman, Lisa Nanovic; University of Wisconsin, Madison, WI, USA

30 A Rare Case of Diabetes Insipidus, Pre-Eclampsia and Acute Fatty Liver in Pregnancy
Aastha Sethi, Surafel Gebreselassie; Wayne State University, Detroit, MI, USA

31 Fanconi's Syndrome Caused by Capecitabine, Irinotecan and Bevacizumab
Aisha Shaikh and Nelson Leung, Mayo Clinic, Rochester, Rochester, Minnesota, USA

32 Severe Hypokalemia and Thyroid Storm Secondary to Iodinated Contrast in a Hispanic Male
Nandita Singh, Naheed Ansari, Anjali Acharya, Jacobi Medical Center, Bronx, New York, USA

33 Conversion to Lanthanum Carbonate Monotherapy Maintains Serum Phosphorus Control and Reduces Tablet Burden in Patients with Chronic Kidney Disease Stage 5
Nirupama Vemuri, South Florida Nephrology Group PA, Coral Springs, FL, USA

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34 Association of Chronic Kidney Disease (CKD) and Anemia with Health Care Services Utilization
Marcus Alexander,[1] Sarita Mohanty,[2] Brian Bradbury,[3] Reshma Kewalramani,[3] Arie Barlev,[3] Denise Globe.[3] [1]Harvard University, Cambridge, MA; [2]Univ. of Southern California, Los Angeles, CA; [3]Amgen Inc., Thousand Oaks, CA

35 Predictors of Consistent In-Target Hemoglobin Over the Transition to Dialysis
Tom Arneson[1], Melissa Skeans[1], Stephan Dunning[1], Michael del Aguila[2], David Gilbertson[1], Allan Collins[1]. [1]Chronic Disease Research Group, Minneapolis Medical Research Foundation, Minneapolis, Minnesota, USA, [2]Roche Laboratories Inc., Nutley, New Jersey, USA

36 Sustained Control of Parathyroid Hormone (PTH), Calcium (Ca), and Phosphorus (P) May Improve Survival in Hemodialysis (HD) Patients
Vasily Belozeroff[1], Mark Danese[2], Karen Smirnakis[1], Kenneth J Rothman[3]; [1]Amgen Inc, Thousand Oaks, CA; [2]Outcomes Insights Inc, Newbury Park, CA; [3]RTI Health Solutions, Research Tri Park, NC, USA

37 Trends in Parathyroid Hormone (PTH) in Hemodiaysis (HD) Patients (PTS)
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38 Trends in the Proportion of Transplantation Among Prevalent Cases of Diabetes-Related End-Stage Renal Disease, By Race, United States, 1995–2004
Nilka Ríos Burrows, Yanfeng Li, Linda Geiss, Desmond Williams, Centers for Disease Control and Prevention, Atlanta, GA, USA

39 The Right Start Knowledge Test: A Kidney Knowledge Survey for Hemodialysis Patients
Kerri Cavanaugh[a], Rebecca Wingard[b], Tom Elasy[a], T. Alp Ikizler.[a] [a]Vanderbilt University Medical Center, Department of Medicine, Nashville, TN. [b] Fresenius Medical Care-NA, Nashville, TN, USA

40 Traditional ESRD Biomarkers May Have Lower Predictive Value for Mortality Than Non-Traditional Biomarkers: A Systematic Review of the Literature
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41 Economic Impact of Cardiovascular Disease and Fractures in Patients with ESRD
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42 Correlates of Chronic Kidney Disease (CKD) Among Hispanic Subgroups: Results from the Kidney Early Evaluation Program (KEEP)
Kenrik Duru[1], Claudine Jurkovitz[2], Andrew Narva[2], Janet McGill[2], George Bakris[2], Shu-Cheng Chen[2], Suying Li[3], Pablo Pergola[2], Peter McCullough[2], Ajay Singh[2], Michael Klag[2], Allan Collins[2], Wendy Brown[2] and Keith Norris[1,2]. [1]Geffen School of Medicine at UCLA, Los Angeles, CA, [2]KEEP Steering Committee, National Kidney Foundation, New York, New York,[3]Chronic Disease Research Group, Minneapolis, MN, USA

43 Underestimation of Chronic Kidney Disease (CKD) by Measured Serum Creatinine: Data from The National Health and Nutrition Examination Survey (Nhanes 1999-2002)
O. Kenrik Duru[1], Dulcie Kermah[2], Allen Nissenson[1], and Keith Norris[1,2]. [1]Geffen School of Medicine at UCLA, Los Angeles, CA; [2]Charles R. Drew University of Medicine/Science, Los Angeles, CA, USA

44 The Association of Iron Administration with Hemoglobin Overshooting
David T. Gilbertson, Rui Zhang, Stephan Dunning, James Ebben, Tom Arneson, Allan J Collins. Chronic Disease Research Group, Minneapolis, MN, USA

45 Moderate Chronic Kidney Disease and Cognitive Function in Adults 20-59 Years of Age (Nhanes III)
Susan M. Hailpern, Michal Melamed, Hillel W. Cohen, Thomas H. Hostetter; Albert Einstein College of Medicine; Bronx, NY USA

46 Use of a Clinical Alert and Reminder System to Promote K/DOQI Bone Guideline Implementation

Daniel Halevy, Iver Juster, Madhavi Vemireddy and Greg Steinberg, ActiveHealth Management, New York, NY, USA

47 Cost-Effectiveness of Epoetin Alfa in Patients on Chronic Kidney Dialysis

Christopher Hollenbeak, Andrew Davies, William M. McClellan, Gregory de Lissovoy. Pennsylvania State University College of Medicine, Hershey, PA; United BioSource Corp, Bethesda MD; Emory University School of Medicine Atlanta, GA, USA

48 Adherence to K/DOQI Guidelines for Bone Metabolism & Disease in Chronic Kidney Disease

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49 Acute Renal Failure and Predictors of Mortality in Patients with Congestive Heart Failure Receiving Nesiritide

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50 Risk Factors for Progression of Kidney Disease: A Longitudinal Study in a Community Practice

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51 Investigation of Nephrogenic Fibrosing Dermopathy and Association with Gadolinium-Containing MRI Contrast

Alexander Kallen[1], Michael Jhung[1], Theresa Hess[1], Steven Cheng[2], George Turabelidze[3], Georges Saab[4], Liana Abramova[2], Matthew Arduino[1], Priti Patel[1]. [1]Division of Healthcare Quality Promotion, CDC, Atlanta, Georgia; [2] Washington University School of Medicine; [3]Missouri Department of Health, St. Louis, Missouri,; and [4] University of Missouri, Columbia, Missouri, USA

52 Bone Mineral Density (BMD) and Chronic Kidney Disease (CKD): Is There a Relationship, a Retrospective Analysis

Kopyt, N; Urffer, SJ; Reed, JF; Paxton, HD, Breitbart, R, Swavely, D; Sterk, K; Jones, K; Etchason, J, Lehigh Valley Hospital, Allentown, PA, USA

53 Association of Chronic Kidney Disease with Birth Weight and Gender in the Kidney Early Evaluation Program Participants

Suying Li[1], Shu-Cheng Chen[1], George Bakris[2], Peter A. McCullough[2], Claudine Jurkovitz[2], Andrew Narva[2], Janet McGill[2], Michael Klag[2], Wendy Brown[2], Keith Norris[2] and Allan Collins[1]. [1]Chronic Disease Research Group, Minneapolis, MN. [2]KEEP Steering Committee, National Kidney Foundation, New York, New York, USA

54 Early Intervention Program: An Evaluation

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55 Kidney Function, Oxidized LDL and Cardiovascular Disease (CVD)

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56 Longitudinal Cost Analysis of Chronic Kidney Patients in Taiwan

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57 Transplantation Hospitalization and Quality of Care for ESRD Patients In Taiwan From 1996-2004

Lih-Wen Mau, Yao-Min Hung, Shang-Jyh Hwang, Herng-Chia Chiu, Allan J. Collins, Robert N. Foley. Unites States Renal Data System Coordinating Center, Minneapolis Medical Research Foundation, Minneapolis, Minnesota, USA. Kaohsiung Medical University, Kaohsiung, Taiwan

58 Prevalence of Ace Inhibitor and ARB Exposure in Acute Kidney Injury in a Tertiry Referral Centre

Finnian R. Mc Causland, Liam F. Casserly, Cornelius J. Cronin; Mid-Western Regional Hospital, Ireland

59 Patient Experience of Chronic Kidney Disease (CKD): Results of a Focus Group Study

Michelle M. Richardson[1], Renee N. Saris-Baglama[2], Milena D. Anatchkova[2], Lesley A. Stevens[1], Dana C. Miskulin[1], Diane M. Turner-Bowker[2], Klemens B. Meyer[1], John E. Ware[2]. [1]Tufts-New England Medical Center, Boston, MA, USA; [2] QualityMetric Incorporated, Lincoln, RI, USA

60 An Analysis of Darbepoetin Dosing Patterns for Treatment of Anemia at a Longterm Acute Care Hospital Setting
E. Sarac, R. Krishnan, M. Gayetsky, L. Madenci, D. Gemmel.; Department of Medicine, St. Elizabeth Center, Youngstown, OH, USA

61 Health-Related Quality of Life Concepts Measured in Chronic Kidney Disease Research
Renee N. Saris-Baglama[1], Alice L. Taubes[2], Michelle M. Richardson[2], Milena D. Anatchkova[1], Diane M. Turner-Bowker[1], Lesley A. Stevens[2], Dana C. Miskulin[2], John E. Ware[1], Klemens B. Meyer[2]. [1]QualityMetric Incorporated, Lincoln, RI, USA; [2]Tufts-New England Medical Center, Boston, MA, USA

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Darren Schmidt[1], James Hall[1], Nahid Islam[1], Tibor Fulop[1], Leandro Mena[2], Harold Henderson[2]. [1]Div. of Nephrology, Dept of Medicine, University of Mississippi Medical Center, Jackson, MS. [2]Div of Infectious Disease, Dept of Medicine, University of Mississippi Medical Center, Jackson, MS

63 Trends in Management of CKD-Related Anemia in The Veterans Health Administration (VHA).
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64 A Cross Sectional Study of Compliance with K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease in an Urban Teaching Clinic
Shahzad Shafique; University of Connecticut, Farmington, USA

65 Hypoalbuminaemia – A Marker of Cardiovascular Disease in Patients with Chronic Kidney Disease Stages II – IV
Nehal Shah MD and Francis Dumler MD.; Division of Nephrology, William Beaumont Hospital, Royal Oak, MI, USA

66 Comorbidities Among Patients with Chronic Kidney Disease
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67 Consistent In-Target Hemoglobin Over the Transition to Dialysis: Effect on Outcomes
Melissa Skeans[1], Tom Arneson[1], Stephan Dunning[1], Michael del Aguila[2], David Gilbertson[1], Allan Collins[1]. [1]Chronic Disease Research Group, Minneapolis Medical Research Foundation, Minneapolis, Minnesota, USA. [2]Roche Laboratories Inc., Nutley, New Jersey, USA

68 Association Between Mortality and Modality in the First 90 Days Following Initiation of Dialysis
Jon Snyder, Yi Peng, Eric Weinhandl, David Gilbertson, Tom Arneson, Allan Collins, Chronic Disease Research Group, Minneapolis, MN, USA

69 The Association of Persistently Low Hemoglobin Levels with Hospitalization and Mortality
Craig A Solid, Eric Weinhandl, David T Gilbertson, Allan J Collins. Chronic Disease Research Group, Minneapolis, MN, USA

70 The Effect of Hyponatremia on The Safety and Efficacy of Nesiritide
Raghava Velagaleti, Leslie Franke, John Clements all affiliated with Synergy Medical Education Alliance, Saginaw, MI, USA

71 Albuminuria and Age as Predictors of Erythropoietin Response in Chronic Kidney Disease
Adam Whaley-Connell, Harbanksh Sangha, Kunal Chaudhary, Georges Saab. University of Missouri-Columbia School of Medicine, Division of Nephrology and Harry S. Truman VA Medical Center, Columbia, Missouri, USA

72 Short-Term Survival Effect of Early Nephrology Care Prior to Dialysis Initiation in Elderly Patients with End-Stage Renal Disease
Yongming Zhao, John M. Brooks, Michael J. Flanigan, Elizabeth A. Chrischilles, Jane F. Pendergast, Lawrence G. Hunsicker; Iowa City, Iowa, USA

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Zimmer Brian, Wentzel Dana, Reed James, Friedman Elliott, Ahmed Basil, Kopyt Nelson. Lehigh Valley Hospital, Allentown, Pennsylvania, USA

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74 Treatment of Idiopathic Membranous Nephropathy (IMN) With the Chinese Herbal *Astragalus Membranaceous (AM)*
Mohammed S. Ahmed, Susan H. Hou, David J. Leehey; Medicine, Loyola University Medical Center, Maywood, IL, USA

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Cherukuri M, Ghali H, Krishnakurup J, Deshmukh V, Belman N, Snyder RW. Easton Hospital/Drexel University College of Medicine, Easton, PA, USA

76 Novel Association of MPGN with Graves' Disease
Christoph Eggert[1], Hatem Amer, Donna Lager[2], Robert Albright [1]; Divisions of Nephrology and Hypertension [1] and Pathology [2] Mayo Clinic, Rochester Minnesota, USA

77 Clinical Predictors of Severity of Proteinuria in a Cohort of Patients with Hepatitis C and Proteinuria
Susan M. Hailpern, Robin Arora, Salman Waheed, Belinda Jim, Anjali Acharya; Jacobi Medical Center and Albert Einstein College of Medicine; Bronx, NY USA

78 The Effect of Combination Treatment with Pegylated Interferonα and Cyclosporin a on Membranoproliferative Glomerulonephritis Induced by Hepatitis C Virus
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79 Membranous Mephropahty in Association with Autoimmune Thyroidits and Unexplained Leukopenia – A New Clinical Syndrome?
Naqi Idris, Hemant Magoo, Sarat Kuppachi, Jinil Yoo Our lady of Mercy Medical Center Bronx, New York, USA

80 A Case of Collapsing FSGS Associated with Still's Disease
Gaurav Jain, Peter Hart, Rahul Pandey, Rubin Bahuva; Cook County Hospital, Chicago, IL, USA

81 Proliferative Glomerulonephritis in a Patient with Angioimmunoblastic T Cell Lymphoma
Kalyana Janga, Subrahmanyam Nasika, Kiran Nakkala, Sheldon Greenberg, Yuanchun Zhou Maimonides Medical center, Brooklyn, NY, USA

82 Podocyte Injury Occurs in the Course of Preeclampsia
Belinda Jim[1], Nandita Singh[1], Naheed Ansari[1], Kisra Anis[1], Anjali Acharya[1], Peter Mundel[2], Yasuhiro Akai[3]
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83 sFlt Upregulates Synaptopodin Expression in Podocytes
Belinda Jim[1], Nandita Singh[1], Naheed Ansari[1], Kisra Anis[1], Kwanghee Kim[2], Peter Mundel[2], [1]Jacobi Medical Center, Bronx, NY, USA, [2]Mount Sinai School of Medicine, New York, NY, USA

84 Anti CD 20 Antibody in the Treatment of Membranous Nephropathy– A Three Case Series
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85 Membranous Nephropathy Associated with Thrombotic Thrombocytopenic Purpura
Sarat Kuppachi, Naqi Idris, Alka Walter and Jinil Yoo

86 Anti-MPO Antibody Small Vessel Vasculitis Presenting as Prostatitis and Nephritis
Jorge Lamarche, Joaquin Rosario, Alfredo Peguero, James A. Haley Veterans Hospital, University of South Florida, Tampa, Florida, USA

87 Atypical Presentation of Thrombotic Microangiopathy
Finnian R. Mc Causland, Liam F. Casserly, Cornelius J. Cronin; Mid-Western Regional Hospital, Ireland

88 Resolution of Steroid-Dependency by a Dairy/Hypoallergenic Diet in Children with Nephotic Syndrome
Majid Rasoulpour, Claire Dalidowitz. Connecticut Children's Medical Center

89 Aortic Thrombosis in an Adult Patient with Minimal Change Nephrotic Syndrome and Hodgkin's Lymphoma: A Rare Association and Complication
E. Sarac, H. Zhang, H. Negrete, J. Spalding, D. Gemmel

90 Nephrotic Syndrome Associated with Chronic Lymphocytic Leukemia
Saeed Shaffi, Khalid Bashir, William Hunter, Creighton university medical center, Omaha, Nebraska

91 Acute Renal Failure Secondary to Severe Type I Cryoglobulinemia Following Rituximab Therapy for Waldenstrom's Macroglobulinemia
Aisha Shaikh and Nelson Leung, Mayo Clinic, Rochester, Rochester, MN, USA

92 Combination Use of ACE/ARB in the Initial Treatment of Loin Pain Hematuria Syndrome
Kate Tretyakov, Adam Dratch, Richard Snyder, Easton Hospital/Drexel University College of Medicine, Easton, PA

93 Effect of Blocking the Renin Angiotensin Aldosterone Sytem (RAAS) on Refractory Focal Segmental Glomerulosclerosis (FSGS) to Lower Blood Pressure and Decrease Proteinuria to Preserve Glomerular Filtration Rate (GFR) and Slow Progression to End Stage Renal Disease (ESRD)
Charanjit Vedi, Kyle Knuppel, Meenal Shah, Allan B. Schwartz, Drexel College of Medicine, Philadelphia, PA

94 Bleeding Complications of Renal Biopsy
Z.Zepceska, S. Dzikova, L. Grcevska, D. Kostadinova, M. Polenakovic, Department of Nephrology, University Clinical Center, Skopje, R. Macedonia

Hemodialysis

95 Line Reversal of Tunneled Dialysis Catheters and Its Impact on Recirculation
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96 Successful Pregnancy Outcome in a Noncompliant Patient on Chronic Hemodialysis (HD)
Ehteshamul Anjum, Ashok Chaudhari, Alf Tannenberg; New York Medical College (Metropolitan) Program, NY

97 Infection Pattern in HIV Infected Hemodialysis Patients
Iram Mahmood Arif, Sheherzad Islam, Monica Grafals, Michael Dunn, Ziauddin Ahmed; *Drexel University College of Medicine, Philadelphia*

98 Effective Hemoglobin (Hb) Control with Epogen (Epoetin Alfa) in the Real-World Clinical Setting
Vasily Belozeroff[1], Karen Smirnakis[1], Steven Johnson[1], Mahesh Krishnan[1]; [1]Amgen Inc, Thousand Oaks, CA

99 Hematide™, A Synthetic Peptide-Based Erythropoiesis Stimulating Agent, Maintains Hemoglobin in Hemodialysis Patients Previously Treated with Epoetin Alfa (EPO)
A Besarab[1], S Zeig[2], R Geronemus[3], P Pergola[4], F Whittier[5], R Zabaneh[6], B Schiller[7], M Kaplan[8], N Levin[9], S Wright[10], S Swan[11], R Wintz[12], D Wombolt[13], R Leong[14], W Lang[14], M Franco[14], and AM Duliege[14]. [1]Detroit, MI; [2]Pembroke Pines, FL; [3]Lauderdale Lakes, FL; [4]San Antonio, TX; [5]Canton, OH; [6]Shreveport, LA; [7]Mountain View, CA; [8]Nashville, TN; [9]New York, NY; [10]Pine Bluff, AR; [11]Minneapolis, MN; [12]Los Angeles, CA; [13]Norfolk, VA; and [14]Palo Alto, CA, USA

100 Uremic Pruritus Patients: A National Survey of Sleep and Mood Disruptions
Sarbani Bhaduri[1], Vandana Mathur[2], Jere Fellmann[1], David Rosen[1] [1]Acologix, Hayward, CA, USA. [2]Mathur Consulting, Woodside, CA, USA

101 Ambulatory Blood Pressure (BP) Monitoring in the Dialysis Population: Is it Essential?
Daphne Bilbrew, Nisleem Islam, Karen Valentine, Tibor Fulop, Mahmoud Salem, Michael Flessener, Darren Schmidt, Nephrology Division, Department of Medicine, University of Mississippi Medical Center, Jackson, Mississippi USA

102 Custom Made Rastermethod for Fistula and Graft
Cees Blokker, EDTNA / LVDT / VAS

103 Assessing the Use of the Calcimimetic Cinacalcet with Low Dose Vitamin D Versus Escalating Doses of Vitamin D Alone in the Treatment of Secondary Hyperparathyroidism (HPT)—The Achieve Study
C Charytan[1], D Corry[2], M Roppolo[3], X Ling[4], J Droge[4], S Fishbane[5]. [1]NY Hosp Med Ctr Queens, Flushing, NY; [2]Olive View UCLA-Med Ctr, Sylmar, CA; [3]Renal Assoc. of Baton Rouge, Baton Rouge, LA; [4]Amgen Inc, Thousand Oaks, CA; [5]Winthrop Univ Hosp, Mineola, NY

104 Sustained Low Efficiency Dialysis (SLED) with Regional Citrate Anticoagulation (RCA) is Without Metabolic Complications, But at the Cost of Increased Calcium Dose
John A. Clark, Gerald Schulman and Thomas A. Golper, Vanderbilt University, Nashville TN, USA

105 Hemodialysis for Hyperammonemia Associated with Ornithine Transcarbomylase Deficiency
Jacob Collen, Jonathan Koff, Kevin Abbott, Nealanjon Das

106 A Randomized, Double-Blind, Cross-Over Design Study of Sevelamer Hydrochloride (SH, Renagel®) and Sevelamer Carbonate (SC) In Chronic Kidney Disease Patients on Hemodialysis

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Winston-Salem, NC; [4]Apex Research of Riverside, Riverside, CA; [5] Genzyme Corporation, Waltham, MA

107 Improving Interdialytic Weight Gain

Noelle Fein, Laura Lindsey, Fresenius Medical Care, Gresham, OR, USA

108 Advance: The Effect of Cinacalcet + Low-Dose Vitamin D on Vascular Calcification in Hemodialysis Patients – Methods

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109 Progress of The Frequent Hemodialysis Network Randomized Trial of In-Center Daily Hemodialysis

Frequent Hemodialysis Network (FHN) Trial Group. NIDDK, NIH, Bethesda, MD, USA

110 The Frequent Hemodialysis Network Randomized Trial of Home Nocturnal Hemodialysis: Change of Trial Design

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111 Permanent Hemodialysis Access in a Suburban End Stage Renal Disease Population

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112 A Time Series Model for Hemoglobin Response in Dialysis Patients on Erythropoietin (EPO)

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113 Vitamin D Deficiency in Dialysis Patients Not on Vitamin D Analog Therapy

Takashi Hato and James Ireland, University of Hawaii John A. Burns School of Medicine Department of Internal Medicine Division of Nephrology Honolulu, Hawaii, USA

114 Distribution and Elimination of ^{45}Ca After Oral Administration of a Calcimimetic in Cynomolgus Monkeys in the Presence or Absence of Calcium Loading

Charles Henley, Edward Shatzen, Fred Lott, David Martin. Metabolic Disorders, Amgen Inc, Thousand Oaks, CA

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Huang, CX[1], Plantinga L[2], Fink NE[2], Melamed ML[3], Klag MJ[2], Powe NR[2]. [1]Johns Hopkins/Sinai Hospital Program in Internal Medicine, [2]Welch Center for Prevention, Epidemiology and Clinical Research, The Johns Hopkins University, Baltimore, MD, USA. [3]Albert Einstein College of Medicine, Bronx, NY, USA

116 Mathematical Modelling of Free Light Chain Removal by Plasma Exchange and Extended Hemodialysis in Patients with Cast Nephropathy
Colin A. Hutchison,[1] Mark Cook,[1] Stephen Harding,[2] Graham Mead,[2] John Hattersley,[4] Neil Evans,[4] Mike Chapel,[4] Paul Cockwell,[1] Arthur Bradwell.[3] [1]Queen Elizabeth Hospital, [2]The Binding Site and [3]University of Birmingham, Birmingham, [4]University of Warwick, Warwick, UK

117 Removal of Free Light Chains by Extended Hemodialysis in Patients with Cast Nephropathy: A Phase 1/2 Clinical Trial
Colin A. Hutchison,[1] Mark Cook,[1] Stephen Harding,[2] Graham Mead,[2] Paul Cockwell,[1] Arthur Bradwell.[3] [1]Queen Elizabeth Hospital, [2]The Binding Site and [3]University of Birmingham, Birmingham, UK

118 Renal Function Recovery Following Velcade and Extended Hemodialysis in Patients with Refractory Multiple Myeloma and Cast Nephropathy: Case Studies
Colin A. Hutchison,[1] Mark Cook,[1] Stephen Harding,[2] Graham Mead,[2] Paul Cockwell,[1] Arthur Bradwell.[3] [1]Queen Elizabeth Hospital, [2]The Binding Site and [3]University of Birmingham, Birmingham, UK

119 Echocardiogram Diagnosis of Pulmonary Hypertension May be Inaccurate in ESRD Pts
Ifeanyi Isaiah, Jesse Goldman, Sung-Ji Schmidt, Sheila Weaver, Jean Lee, Temple University Divisions of Nephrology and Pulmonary

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Manasvi Jaitly, Sumit Mohan, Muhammad Mujtaba, Herman Anderson, Jen-Tse Cheng, Velvie Pogue. Harlem Hospital, NY

121 An Innovative Approach to Glycemic Control in ESRD Patients (Pts)
Kalyana Janga, Sheldon Greenberg, Miriam Greenberg, Saurabh Goel, Subrahmanyam Nasika; Maimonides Medical Center, Brooklyn, NY

122 Dialysis Patients are at Risk of Being Undermedicated During Hospital Stay
Charles Jere, Mehbeen Khan, Ryan Chowdhury, Monica Grafals, Karthik Ranganna, Ziauddin Ahmed; Department of Medicine, Drexel University College of Medicine

123 Frequency of Hemoglobin (Hb) Monitoring in Dialysis Units is Associated with Facility-Level Hb Variability
Irfan Khan and Mahesh Krishnan. Amgen Inc., Thousand Oaks, CA

124 Elevation of C-Reactive Protein Leads to Higher Epogen Dosing and Worse Nutrional Status in Hemodialysis Patients
Nitin Khosla, Sharon Soroko, Sam Kuo, and Ravindra Mehta, University of California At San Diego, San Diego, CA, USA

125 Effect of Hepatitis C Infection on Anemia in Hemodialysis Patients
Anand Khurana, Mohanram Narayanan, Allan E Nickel; Nephrology, Texas A & M University, Temple, TX, USA

126 Comparative Characterization of the New Baxter Xenium 170 Dialyzer (BX)
Detlef H Krieter[1], Horst-Dieter Lemke[2], Christoph Wanner[1]; [1]University Hospital Würzburg, Germany; [2]EXcorLab GmbH, Obernburg, Germany

127 Comparison of Prophylactic Antibiotics in Tunneled-Catheter Manipulation in Dialysis Dependent Patients
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128 The Cardio-Renal-Anemia Syndrome (CRA) in Hemodialysis Patients
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129 Intensive Education as a Quality Improvement Tool to Reduce Interdialytic Weight Gain (IDWG) in Chronic Hemodialysis (CHD) Patients
Jeanette McLaughlin; Katrina Hebert; Tammy Poma; Nicole Stankus

130 Early Detection of Arteriovenous Fistula Stenosis by Doppler Ultrasonography (DUS)
Shikha Mehta, Mark E. Lockhart, Rachel Oser, Michelle L. Robbin, Michael Allon. The University of Alabama at Birmingham, Birmingham, AL, USA

131 High Dose Paricalcitol Therapy Used to Decrease iPTH > 4000 pg/ml
Susan Morrison, Cynthia Wommack, Robert Cuddihee. Affiliated Hospitals Dialysis Center, St. Louis, MO, USA

132 Blood Volume Monitoring Improves Volume Assessment and Management as Determined By Cardiovascular Parameters
Luana Pillon, Chi-Hong Tseng: New York University School of Medicine, New York, NY, USA

133 Can Oral Supplementation With a Collagen-Casein Based Hydrolized Liquid Protein Improve Serum Albumin Levels in Hypoalbuminemic Hemodialysis Patients?
Ann Pittaoulis, Evelyn Phillips, Adriana Popovici, Mary Anne Rocks, Kelly Lynn; Philadelphia, PA, USA

134 Mental Score is Better than Physical Score in a Health Survey of Dialysis Patients
Ishmael Qattash, Maliha Ahmed, Ahmed Mian, Jean Lee, Ziauddin Ahmed
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135 Serum Fructosamine (SF), An Alternative Marker of Glycemic Control, Predicts Hospitalization and Infection in Diabetic Hemodialysis (DMHD) Patients (Pts) Better Than Hemoglobin A1c (HbA1c)
Muhammad A. Rafiq, Neal Mittman, Hina Chaudhry, Lalathaksha Kumbar, Brinda Desiraju, Morrell M. Avram. Avram Division of Nephrology, Long Island College Hospital, Brooklyn, NY, USA

136 Vasopressin Response in Intradialytic Hypotension
Mira Rho, Mark A. Perazella, Aldo Peixoto, Chirag Parikh, Ursula C. Brewster, Section of Nephrology, Yale University School of Medicine, New Haven, CT, USA

137 Effectiveness of Ultrasonography Vein Mapping for the Creation of AV Fistula
Joseph Saggio, Ismail Qattash, Michael Weingarten, Karthik Ranganna, Ziauddin Ahmed. Department of Medicine and Department of Surgery, Drexel University College of Medicine. Philadelphia, PA USA

138 Nephrogenic Fibrosing Dermopathy in a Patient with Multiple Myeloma and Bone Marrow Transplant
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139 A Simple Feedback Tool to Enhance Patient Education on Advance Directives
Marcia Sawyer, Botsford Kidney Center, Livonia, MI, USA

140 Intradialytic Parenteral Nutrition (IDPN): Changes in Albumin, Total Protein, Dry Weight, Bun, and Creatinine after 3 to 12 Months of Therapy
Deborah Scholl, Richard Dowling, Michelle Ricker, Stan Lindenfeld; Pentec Health, Inc., Boothwyn, PA, USA

141 Dialysis Dose Delivery in Hospitalized Patients with Acute Kidney Injury
Shamik H Shah, Sharon Soroko, Ravindra L Mehta, University of California, San Diego, CA, USA

142 Evaluation of the Nutritional Status According to Essential Amino Acid Intake in Hemodialysis Patients
Cheong Min Sohn, Su An Kim, Kim, Hye Jin. Dept. of Nutrition care service, Seoul National University of Bundang Hospital, Gumi-dong, Bundang-gu, Seongnam-Si, Gyeonggi-do, Korea

143 Treatment with Oral Paricalcitol Reduces Total and Bone-Specific Alkaline Phosphatase in Dialysis Patients
Stuart Sprague[1], Joel Melnick[2], Sandy Fukumoto[2], Richard Hippensteel[2], Vicky Blakesley[2], and Jin Tian[2]. [1]Feinberg School of Medicine, Northwestern University, Evanston, IL, USA; [2]Abbott Laboratories, Abbott Park, IL, USA

144 Quotidian Short Home Hemodialysis; Comparing Two Techniques at the Dialysis Center Of Lincoln
L Spry, M Buss, M Carver, and J Carder. Lincoln, NE, USA

145 Severe Hypercalcemia in a Hemodialysis Patient
Balaji Srinivasan, Gundersen Lutheran Hospital, LaCrosse, WI, USA

146 Serum Prealbumin in the Dialysis Population
Jen Strong, Les Spry, Alison Steiber, Teresa Gerbeling, Jackie Carder; Dialysis Center of Lincoln, Inc., Lincoln, Nebraska, USA

147 The Relationship of Serum Albumin to Serum Prealbumin in the Dialysis Patient
Jen Strong, Les Spry, Alison Steiber, Teresa Gerbeling, Jackie Carder; Dialysis Center of Lincoln, Inc., Lincoln, Nebraska, USA

148 Dietary Pitfall of Christmas Eve and New Year's Eve on Weekends in Patients Undergoing Maintenance Hemodialysis
Kimiko Takahashi, Emi Kihara, Seiji Kawahara, Nanako Ikari, Kazuko Arita, Katsutoshi Maeda and Hiroaki Oda; Oda Medical Clinic, Hiroshima, Japan

149 Carnitine Effectiveness on Intradialytic Hypotension
Joel M. Topf, and Genevieve Alumit. St. John Hospital & Medical Center, Detroit, Michigan, USA

150 Promoting Self-Care in Hemodialysis
Tracey Tyus-Bailey, Kristie Lewis; Greenfield Health Systems, Bingham Farms, MI, USA

151 Retrospective Evaluation of Vectra Grafts vs. PTFE Grafts for Hemodialysis Patients
Janice Weatherspoon, Ivan Maya, Carlton Young, Michael Allon. University of Alabama at Birmingham. Divisions of Nephrology and Transplant Surgery. Birmingham. AL, USA

152 The Assocation Between Glycosylated Hemoglobin (HgbA1c) and Three-Year Mortality Risk in Patients on Maintenance Hemodialysis
M Williams, Harvard Medical School, Boston, MA, USA; E Lacson Jr., M Teng, JM Lazarus, R Hakim, Fresenius Medical Care, Lexington, MA, USA

153 Looking Through the Fishbowl: Lessons Learned From the CAHPS ICH Quality Improvement Project
Dawn Wilson, DaVita Covington Dialysis, Covington, Virginia, USA

154 Reasons for Hemodialysis Catheter Use & Its Complications: Patient and Coordinator Perspectives
Jane Yuan, Dheeraj Rajan, Cynthia Bhola, Julia Lee, Charmaine E. Lok; University of Toronto & Toronto General Hospital, Toronto, Ontario, Canada

Hypertension

155 Generalized Vasoconstriction and Acute Hypertension Produced By the Calcimimetic, Cinacalcet, In Uremic and Normal Rats
Ryan M. Fryer, Jason A. Segreti, Kristin A. Koch, Masaki Nakane, J. Ruth Wu-Wong, Glenn A. Reinhart; Integrative Pharmacology, Abbott Labs, Abbott Park, IL, USA

156 Genetic Variation Within Adrenergic Pathways Determines *In Vivo* Effects of Presynaptic Stimulation in Humans
Maple M Fung, Carie Nguyen, Parag Mehtani, Rany M. Salem, Brandon Perez, Brenda Thomas, Daniel T. O'Connor. University of California at San Diego, La Jolla, CA, USA

157 Hyperhomocysteinaemia and Type IV Hypertriglyceridaemia are Common Cardiovascular Risk Factors in Hypertensives
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158 The Relationship Between Blood Pressure, Obesity, Endothelin-1 and Plasma Lipids in a Gulf Arab Population
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159 Prevalence of White Coat Effect in Hemodialysis Patients as Determined By a Standardised Automated Blood Pressure Measurement
Manish M Sood, Marisa Battistella, Charmaine E. Lok, Robert Richardson. Toronto, Ontario, Canada

160 Protective Role of AT_1 Blockade in Renal Tissue in Uninephrectomized SHR & WKY Rats
Toblli Jorge; Cao Gabriel, Angerosa Margarita; Laboratory of Experimental Medicine. Hospital Alemán. Buenos Aires

161 Hypertension Prevalence in Chinatown Clinic
Seung J. Yi, Lisa K. Wong, Vincent J. Zarro and Allan B. Schwartz. Drexel Univ College of Medicine, Philadelphia, PA, USA

Peritoneal Dialysis

162 Focused Techniques Can Impact Peritonitis Rates: Making the ISPD Goal Achievable
Michelle Bloom, Rai Care Center, Fairview Heights, IL, USA; Jay Seltzer, Rai Care Center, Fairview Heights, IL, USA; Michelle Hofmann, Baxter healthcare, St. Louis, MO, USA

163 Automated Peritoneal Dialysis is Associated with Poor Response to Hepatitis-B Vaccination
Fakhar Ijaz, Satyaki Banerjee, Umapati Hedge, Cynthia Newton, Michael Baggett, Irfan Sohail, Fatima Syed, Muhammad G. Alam

164 Efficacy of Hepatitis-B Vaccination in Patients Maintained on Peritoneal Dialysis
Fakhar Ijaz, Satyaki Banerjee, Umapati Hedge, Cynthia Newton, Michael Baggett, Irfan Sohail, Fatima Syed, Muhammad G. Alam

165 "PD" Peritoneal Dialysis or Personal Dedication
Talha H Imam, Kaiser Permanente, Fontana, California, USA

166 Pulmonary Hypertension (PH) is Prevalent in Peritoneal Dialysis (PD) Patients (Pts) As Well As Hemodialysis (HD) Pts
Lalathaksha Kumbar, Neal Mittman, Paul A Fein, Muhammad A Rafiq, Jyotiprakas Chattopadhyay, Morrell M Avram. Avram Division of Nephrology, Long Island College Hospital, Brooklyn, New York, USA

167 Efficacy of Icodextrin in Peritoneal Dialysis Patients: A Systematic Review
Mohan Sengodan, Sangeetha Radhakrishnan. Department of Medicine, Unity Health System, Rochester, NY and PSG Medical College, Coimbatore, India

Progressive Kidney Disease

168 Long Term Follow Up in Fabry Patients with Proteinuric Kidney Disease
F Breunig, A Emmert, F Weidemann, J Strotmann, C Wanner. University of Würzburg, Germany

169 African Americans' Knowledge and Behavior Regarding Early Detection of Kidney Disease
Teri Browne[1], Amy D. Waterman[2], Elisa H. Gladstone[3], & Brian M. Waterman[4]
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170 Clinical Inertia and Cardiovascular Disease (CVD) Risk Factor Modification in Chronic Kidney Disease (CKD)
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171 Group Versus Individual Appointments and Their Impact on Kidney Disease Progression in Type 2 Diabetes Patients Who Attend The Cleveland Clinic Florida
Norma Gonzalez, Laura Byham-Gray, Robert Denmark, Michelle Wein, Riva Touger Decker

172 Fabry Disease & The Kidney: The University of Connecticut Experience
Lalarukh Haider, Robert M Greenstein, Nancy Day Adams. University of Connecticut Health Center, Farmington, CT, USA

173 Unique Receptor Interaction Prolongs the In Vivo Half-Life of Continuous Erythropoietin Receptor Activator
Anton Haselbeck, Michael Brandt, Michael Jarsch; Roche Diagnostics GmbH, Penzberg, Germany

174 Chronic Kidney Disease Patients and Renal Transplant Recipients Have an Increased Incidence of Monoclonal Gammopathies
Colin A. Hutchison,[1] Stephen Harding,[2] Graham Mead,[2] John Townsend,[1] Martin Landray[4], Paul Cockwell,[1] Arthur Bradwell.[3] [1]Queen Elizabeth Hospital, [2]The Binding Site and [3]University of Birmingham, Birmingham, [4]Radcliffe Hospital, Oxford, UK

175 Computerized Anemia Management Program (CAMP©) Dosing of Once Monthly De Novo Darbepoetin Alfaversus Bodyweight-Based Dosing
Khaled Ismail, Elias Chalhoub, Ramy Fayad, Mark D. Faber, Stanley Frinak, Jerry Yee. Henry Ford Hospital, Detroit, MI, USA

176 Impact of Co-Insurance on Out-Of-Pocket Cost Burden for Patients With Chronic Kidney Disease
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177 Higher Hemoglobin Targets and Kidney Disease Progression: A Systematic Review
Sankar D Navaneethan, Giovanni FM Strippoli. University of Rochester, NY; Cochrane Renal Group, Sydney, Australia

178 Factors Influencing Nephrology Referral in Moderate to Severe Chronic Kidney Disease
Aide Onime, Robert White, Karen Servilla, Antonios Tzamaloukas, Clifford Qualls, New Mexico VA Health Care System and University of New Mexico, Albuquerque, NM, USA

179 RAAS Blockade Causing Renal Failure in CKD Patients with Renal Artery Stenosis: A Prospective Mayo Health System Clinic 50-Month Analysis
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180 Renal Failure from RAAS Blockade in CKD Patients: A Prospective 50-Month Analysis - A Call For Pragmatic Caution to Optimize Cardiorenal Protection with RAAS Blockade
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181 Chronic Kidney Disease (CKD) in Patients with Nephrolithiasis: Expanded Data
Rute Paixao, MD, Mauro Braun, MD, John B Copley, MD, Beth L Fromkin, MD, Arun Amatya, MD [1]Nephrology and Hypertension, Cleveland Clinic Florida, Weston, FL, United States

182 NGAL and Extracellular Matrix Proteins in TGF-Beta Induced Chronic Renal Fibrosis
Ponda M, Siconolfi-Baez L, Kopp JB, Angeletti RH, Hostetter TH, Bitzer M.; Albert Einstein College of Medicine, Bronx, NY; NIDDK, Bethesda, MD

183 Effect of Pharmacological Suppression of Secondary Hyperparathyroidism on Cardiovascular Hemodynamics in Predialysis CKD Patients – A Preliminary Observation
Vaibhav Sahni,[1] Narinder P Singh[2] . [1]Drexel University College of Medicine, Philadelphia, PA, USA. [2]MAM College, New Delhi, India

184 Safety and Tolerability of C.E.R.A. (A Continuous Erythropoietin Receptor Activator) In Patients with Chronic Kidney Disease: Pooled Data from Ten Phase II-III Trials
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185 Four-Year Follow-Up of a Cohort of Patients with Advanced CKD Managed in an Academic CKD Clinic: Grounds for Optimism
Andres Serrano, Jenny Huang, Laura Nishi, Rajani K. Chilakapati, Cybele Ghossein, James Paparello, Shubhada Ahya, Neenoo Khosla, Robert Rosa, Melissa Weitzel, Daniel Batlle. Division of Nephrology/Hypertension, Feinberg School of Medicine of Northwestern University, Chicago IL, USA

186 Frequency of Hb Testing and Anemia Diagnosis in Patients with Chronic Kidney Disease During Pre and Postdialysis Period
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187 Unmasking of Periodic Limb Movements in Sleep During Treatment of Sleep Apnea with Continuous Positive Airway Pressure (CPAP) in the Chronic Kidney Disease Population
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Transplantation

188 Pseudo Transplant Renal Artery Stenosis as a Cause of Renal Impairment in a Patient with Kidney Transplant
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189 Concurrent Acute Recurrent Renal Allograft Rejection, BK Nephropathy/Viremia & Osmotic Acute Renal Failure: A Case Report
Amatya Arun MD, Braun Mauro MD, Copley J Brian,MD, Fromkin Beth MD, Paixao Rute, MD. Cleveland Clinic, Weston, Florida, USA

190 Lack of Benefit from Bumetanide Infusion After Cadaveric Kidney Transplantation
Piyaporn Apivatanagul, Svastijaya Daviratanasilpa, Charnes Chiu, Lon Sadowsky, Shiang-Cheng Kung, Rasib Raja, Albert Einstein Medical Center, Philadelphia, PA, USA

191 There is no Free Lunch: The Negative Consequences of Taking Cyclosporine with Food
Rodolfo Batarse, Linda Awdishu, Alex Dominguez, James Lane, Robert Steiner. UCSD Medical Center, San Diego, CA, USA

192 Primary Amyloidosis in a Renal Transplant Recipient: A Case Report
Ruchika Batwara, Sharath Subramanian, Parameswaran Hari, Syed Hussain. Medical College of Wisconsin, Milwaukee WI, USA

193 Recurrence of Scleroderma Renal Crisis in a Kidney Transplant Patient with Antecedent Corticosteroid Use
Ruchika Batwara, Nidhi Aggarwal, Brahm Vasudev. Medical College of Wisconsin, Milwaukee, WI, USA

194 Economic Impact of Gastrointestinal Medication Reduction After Conversion From Mycophenolate Mofetil (MMF) To Enteric-Coated Mycophenolate Sodium (EC-MPS)
Paul Bolin, Karen Parker, and Susan Gerkin

195 Social Networks and African American Pathways to Kidney Transplantation
Teri Browne, University of Chicago, School of Social Service Administration, Chicago, IL, USA

196 Non-Serogroup O1 *Vibrio Cholerae* in a Renal Transplant Patient
Micah R. Chan, John D. Pirsch, University of Wisconsin and Affiliated Hospitals, Madison, WI, USA

197 Impact of Anemia Pre and Post-Transplant on Patient Survival
Darshika Chhabra[1,3], Michele Parker[2], Jayant Patel, MD[1,3], Maliha Syed, MD[1,3], Satinder Oberoi, MD[1,3] and Lorenzo Gallon, MD[1]. [1]Nephrology/Transplantation, Northwestern University, Chicago, IL, USA; [2]Cardiology, Duke University, Durham, NC, USA and [3]Internal Med., Michael Reese Hospital, Chicago, IL, USA

198 Impact of Anemia Pre and Post-Transplant on Renal Allograft Survival and Acute Rejection Rates
Darshika Chhabra[1,3], Michele Parker[2], Jayant Patel, MD[1,3], Maliha Syed, MD[1,3], Satinder Oberoi, MD[1,3] and Lorenzo Gallon, MD[1]. [1]Nephrology/Transplantation, Northwestern University, Chicago, IL, USA; [2]Cardiology, Duke University, Durham, NC, USA and [3]Internal Med., Michael Reese Hospital, Chicago, IL, USA

199 Metabolic Syndrome in an Outpatient Transplant Clinic Population
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200 Single Center Experience with Low-Dose Thymoglobulin and Steroid Free Induction Immunosuppression in Kidney Transplant Patients
Chhavi Gupta, Adit Mahale, Mythili Ghanta, Brian Mceever, Gopal K Chemiti, Thomas Ahlin, Bhargav M Mistry; Department of Nephrology and Transplantation, MeritCare Medical Group, Fargo, ND, USA

201 Depression, Social Support and Medication Self-Efficacy in Older Renal Transplant Recipients
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202 Rhabdomyolysis as Complication of Ehrlichiosis in a Renal Transplant Recipient
Roy Jhagroo[1], Nayan Gowda[1], Christine Vigneault[1], Gautam Bhimidi[1], Mathew Brown[2], Anne Lally[2], David Hull[2], K. Vinay Ranga[1,2,] University of CT Health Center, Farmington, CT[1] / Hartford Hospital, Hartford, CT[2]

203 Leukopenia in Renal Transplant Recipients, Risk Factors and Complications
Ali R Khan, MD[1], Anita Patel, MD[1], Moushen AlHakeem, MD[1], Mariella Goggins, MD[1], Ravi Parasuraman, MD[1], Vanji Karthikeyan, MD[1] and K K Venkat, MD[1]. [1]Nephrology, Henry Ford Hospital, Detroit, MI, USA

204 Single Center Experience with Low-Dose Thymoglobulin in Kidney Transplant Patients
Adit Mahale, Mythili Ghanta, Chhavi Gupta, Brian Mceever, Gopal Chemiti, Thomas Ahlin, Bhargav Mistry; Department of Nephrology and Transplantation, MeritCare Medical Group, Fargo, ND, USA

205 Quality of Life Responses from Living Related, Emotionally Related and Publicly Solicited Live Kidney Donors of Diverse Ethnicities
Mary McKinney and Patricia McDonough Montefiore Medical Center Bronx, NY

206 Management of Anemia in Post-Transplant Patients with Darbepoetin Alfa

KM Ratanavanich, JH Veis, S Loughlin, J Moore. Section of Nephrology, Washington Hospital Center, Washington DC USA

207 Hypomagnesemia Leading to Blindness in a Renal Transplant Patient
Syed Saghir, Farhan Arif, Michael Cardi, The Christ Hospital, Cincinnati, OH, USA

208 ANCA Positive Recurrent IgA Nephropathy Post Transplantation
Sein Yin See[1], Roy Jhagroo[1], Christine Vigneault[1], Mathew Brown[2], Anne Lally[2], David Hull[2], K.Vinay Ranga[1,2]; University of Connecticut, Farmington, CT[1]/ Hartford Hospital Hartford, CT[2]

209 Thymoglobulin Induction for the Double Avoidance of Steroids and Calcineurin Inhibitors in Living-Related Kidney Transplantation
Hasan Shahab, MD, Mathew Pyenta DO, David Butcher MD, Mohamed El-Ghoroury MD

210 Polyoma Virus Infection in 192 Kidney Transplant Patients Utilizing an Alemtuzumab Induction- Steroid-Free Protocol
Shammas A, Najafi A, Tadzong B, Light J, Veis J, Mehta T, Lawsin L, Moore, J. Division of Nephrology and Transplant Services, Washington Hospital Center (WHC), Washington DC, USA

211 Effect of Sirolimus Versus Mycophenolate Mofetil on The Efficacy of Darbepoetin Alfa On Anemia in Renal Transplant Recipients
Shamin Vania, Sandeep Jaglan, Karthik Ranganna, Ziauddin Ahmed, Sandra Levison, Drexel University College of Medicine, Philadelphia

212 Early and Aggressive Recurrence of Idiopathic Membranous Nephropathy in a Renal Transplant Recipient
Tausif Zar[1], Sein Yin See[1], Fabiola Balarezo[1], Nimrata Ghuman[1], Rigoberto Gonzalez[1], Karen McHugh[2], Mathew Brown[2], Anne Lally[2], David Hull[2], K.Vinay Ranga[1,2] .University of Connecticut ,Farmington, CT[1]/ Hartford Hospital Hartford, CT[2]

Other

213 Effect of Baseline Estimated Glomerular Filtration Rate (eGFR) on The Efficacy of Once-Monthly (QM) Darbepoetin Alfa in the Maintenance of Hemoglobin (HB) Levels in Patients with Chronic Kidney Disease (CKD)
Anil Agarwal,[1] Chao-Yin Chen,[2] Preston Klassen,[2] Reshma Kewalramani[2] [1]Ohio State University, Columbus, OH, USA; [2]Amgen Inc., Thousand Oaks, CA, USA

214 Cardiac Troponin I Has Low Negative Predictive Value for the Detection of Occlusive Coronary Artery Disease in Patients with Renal Failure
Saravanan Balamuthusamy Lavanya Srinivasan Meka Srinivasa Suresh Hathiwala Sandeep Khosla Earl Smith

215 Statins Decrease the Risk of Myocardial Infarction, Coronary Heart Disease and Vascular Events in Patients with Renal Failure. A Meta-Analysis
Saravanan Balamuthusamy, Janos Molnar, Suresh Hathiwala, Nandana Mapakshi, Arjun Das, Nishant Jalandara Earl Smith; Rosalind Franklin university/Chicago Medical School

216 An Examination of Direct and Indirect Employer Costs Associated with Epoetin Alfa Treatment in Pre-Dialysis Chronic Kidney Disease Patients
Brahim K. Bookhart[3], Frank Papatheofanis[1], Namrita Chawla[2], Erik Muser[3], Catherine Tak Piech[3]; [1]UCSD, San Diego, CA, USA; [2]Aequitas, San Diego, CA, USA; [3]Ortho Biotech Clinical Affairs, LLC, Bridgewater, NJ, USA

217 A Double-Blind, Placebo-Controlled, Randomized Phase Iii Study of the Safety of Ferumoxytol as a New Intravenous Iron Replacement Therapy
Louis Brenner[4], Ajay Singh[1], Joachim Hertel[2], Marializa Bernardo[3], Jovanna Baptista[4], Annamaria Kausz[4], Brian Pereira[4]. [1] Brigham and Women's Hospital, Boston, MA, USA; [2]University Hospital Medical Center, Augusta, GA, USA; [3]Southwest Houston Research, Houston, TX, USA; [4]Advanced Magnetics, Inc. Cambridge, MA, USA

218 Safety and Efficacy of Ferumoxytol as an Intravenous Iron Replacement Therapy: Results From a Phase III Study of Chronic Kidney Disease (CKD) Patients Not on Dialysis
Louis Brenner[4], Bruce Spinowitz[1], Marializa Bernardo[2], Sylvia Noble[3], Jovanna Baptista[4], Brian Pereira[4]. [1]New York Hosp Med Ctr of Queens, Flushing, NY, USA; [2]Southwest Houston Research, Houston, TX, USA; [3]Northwest Louisiana Nephrology, Shreveport, LA, USA; [4]Advanced Magnetics, Inc. Cambridge, MA, USA

219 Long-Term Followup of Patients with Anemia of CKD Treated with Once Monthly (QM) De Novo Darbepoetin Alfa (DA)
Elias Chalhoub, Khaled Ismail, Mark D. Faber, Rami Fayad, Stanley Frinak, Jerry Yee. Henry Ford Hospital, Detroit, MI, USA

220 Efficacy of Cholecalciferol (Vitamin D_3) Therapy in Correcting Vitamin D Insufficiency and Secondary Hyperparathyroidism in Patients with Chronic Kidney Disease: A Randomized, Placebo Controlled Study
Prakash Chandra[‡], Thomas R. Ziegler[‡] Lynn E. Schlanger*, Wenli Wang*, James T Someren*, and Vin Tangpricha[*‡]; Departments of [*] Medicine, and [‡] Graduate Program in Nutrition and Health Sciences, Emory University, Atlanta, GA, USA*

221 Lack of Association of Conventional Cardiovascular Screening Tests with Survival of Patients on Hemodialysis (HD)
Mona Doshi, Detroit, MI, Charles Herzog, Minneapolis, MN & Lawrence Hunsicker, Iowa City, IA, USA

222 C.E.R.A. Once Monthly Maintains Stable Hb Levels in Patients with CKD on Dialysis with and Without Congestive Heart Failure (CHF)

Steven Fishbane, Allen Nissenson, University of California, Los Angeles, CA, USA. Ambrose Kwok, Everest Clinical Research Services, Markham, Ontario, Canada. Richard Beswick, Roche Laboratories, Nutley, NJ, USA. Winthrop University Hospital, Mineola, NY, USA

223 Efficacy of C.E.R.A., A Continuous Erythropoietin Receptor Activator, In Treatment of Renal Anemia: Overview of 6 Global Phase 3 Trials
Steven Fishbane[1], Cheryl Dalton[2], Richard Beswick[3], Paula Dutka[1], Rebecca Schmidt[2]
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224 Barriers to Food Acquisition in Hemodialysis Patients
Teresa Gerbeling, Jackie Carder, Tammy Burton-Fikar, Jen Strong. Dialysis Center of Lincoln, Inc., Lincoln, Nebraska, USA

225 Denovo Monthly Dosing with Darbepoetin Alfa
Robert P. Geronemus and Rachel Geronemus, South Florida Nephrology Associates, Lauderdale Lakes, FL, USA

226 The Endothelial Pattern of Injury in Glomerulopathies (GP) as Assessed by the Immunohistochemical (IHC) Expression of Von Willebrand Factor(VWF), CD 31 and CD 34
C Gluhovschi, G. Gluhovschi, E. Potencz, D. Herman, V.Trandafirescu, A. Schiller, L. Petrica, S. Velciov, G. Bozdog, F. Bob, C. Vernic, V.Guset, C. Muntean, D.Cioca, Nephrology, Univ. of Medicine and Pharmacy, Timisoara, Romania

227 Do Prophylactic Antibiotics Ensure Protection in the Surgical Cure of Dental Foci in Patients with Chronic Glomerular Disease as Assessed by the Dynamics of Urinary N-Acetyl-β-D-Glucosaminidase (NAG)?
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228 Screening for Chronic Kidney Disease in Human Immunodeficiency Virus: The Renal Clinic Perspective
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267 Permanent Exposure of a Cryptic Actin Binding Site In FSGS-Causing Mutant Alpha-Actinin-4
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A CASE OF BIOPSY PROVEN SPONTANEOUS CHOLESTEROL EMBOLISM

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The kidney is a frequent target for cholesterol crystal embolization (CCE). Most cases of diagnosed cholesterol emboli syndrome follow intravascular procedures where blood vessel manipulation or trauma disrupts the fibrous cap of an atherosclerotic plaque showers cholesterol crystals down stream. CCE also can occur without preceding vascular procedures and has been termed spontaneous CCE. Anti-coagulation is a known risk factor for this condition. Atheroembolic renal disease (AERD) is the syndrome of acute renal failure following CCE. It is often irreversible, with significant morbidity and mortality.

We present the case of a 73 year-old Caucasian male with a past medical history of hypertension and CKD (creatinine 4.0 mg/dL), who presented to the hospital with weakness. The patient had no history of angiographic or vascular procedures or anticoagulation. On physical examination the patient had livedo reticularis in both lower extremities and multiple purple toes. The remainder of the physical exam was unremarkable. Laboratory data showed a creatinine of 7.2 mg/dL, WBC 8200/mm3 with 12% eosinophils, Hgb 11.2 g/dL, erythrocyte sedimentation rate >140mm/hr and normal complements. Urine analysis showed coarse granular casts. AERD was suspected and a renal biopsy showed intra-arterial luminal clefts and focal dense infiltration of eosinophils confirming the diagnosis of AERD.

Subsequently, the patient became dialysis dependent and remains on dialysis.

Our observation describes a patient with advanced CKD who developed spontaneous AERD. We could identify no risk factors beyond diffuse atherosclerosis. We discuss the diagnosis and review the literature on spontaneous CCE.

SYNDROME OF TUBULOINTERSTITIAL NEPHRITIS AND UVEITIS: A UNIQUE ENTITY OR EXAMPLE OF EXTRA-PULMONARY SARCOIDOSIS

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Granulomatous interstitial nephritis (GIN) is found in only 0.5% of kidney biopsies. A limited number of diseases can cause GIN. In contrast, occulorenal syndrome has a broad differential. The intersection of occulorenal syndrome and GIN has only three diagnostic possibilities: sarcoidosis, Wegeners granulomatosus and tubulointerstitial nephritis and uveitis syndrome (TiNU). We describe a case of biopsy proven TiNU, review the literature and discuss the possibility of TiNU being a variant of renal-limited sarcoidosis.

A 24 year old, previously healthy, African American woman presented to the hospital with fatigue and eye pain. Her ocular examination showed anterior uveitis. Otherwise the physical examination was unremarkable.

Laboratory tests revealed a creatinine of 3 mg/dl. Urine analysis showed benign sediment with a spot protein:creatinine ratio of 0.6. Erythrocyte sedimentation rate was 65 mm/h, hemoglobin was 6.2 g/dl and serum complements were normal. Hepatitis, HIV and ANCA serologies were all non-reactive. Antistreptolysin titres were modestly elevated at 210 (0-200). ACE level and calcium levels were normal. A chest X-ray and renal ultrasound were unremarkable.

The patient’s renal function deteriorated and her creatinine peaked at 6.7 mg/dL on hospital day 5. A renal biopsy was performed and was consistent with GIN. The biopsy and previous diagnosis of anterior uveitis lead to a diagnosis of TiNU. The patient was started on oral and ocular steroids. Renal function improved dramatically and vision slowly improved. She currently has normal renal and normal vision.

Only 118 biopsy proven cases of TiNU have been reported in the literature. Renal-limited sarcoidosis has rarely been reported. We speculate that TiNU and sarcoidosis are similar diseases, presenting with simultaneous renal and ocular manifestations given the similar histology and response to steroids. Better understanding of the pathophysiology of these diseases will help solve this diagnostic dilemma.

RECURRENCE OF SCLERODERMA RENAL CRISIS IN A KIDNEY TRANSPLANT PATIENT WITH ANTECEDENT CORTICOSTEROID USE.

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We report an unusual case of recurrent scleroderma renal crisis (SRC) in a renal allograft recipient, possibly due to initiation of high-dose prednisone.

A 56-year-old woman with history of end-stage renal disease due to SRC presented with dyspnea, hypotension and new onset renal dysfunction. She underwent zero mismatch pediatric en-bloc renal transplantation two years ago. She was diagnosed with post-transplant lymphoproliferative disorder (PTLD) a month ago. At that time her immunosuppression was changed from tacrolimus and mycophenolate mofetil to tacrolimus and high-dose prednisone.

On admission, she was hypotensive and required vasopressors. Physical examination revealed jugular venous distension and pedal edema. Laboratory evaluation was significant for a BUN of 51 mg/dL and creatinine of 2.4 mg/dL (baseline 1.1 mg/dL). Echocardiogram and right heart catheterization revealed new onset severe pulmonary hypertension. She was managed with diuretics and vasopressin for heart failure, and intravenous epoprostenol and sildenafil for pulmonary hypertension. Despite improvement in cardiac output with this regimen, her renal function continued to worsen, necessitating continuous veno-venous hemofiltration (CVVH). A renal transplant biopsy was performed which demonstrated narrowed arteriolar lumens, fibrinoid necrosis and microthrombi, consistent with SRC. CVVH was changed to slow intermittent hemodialysis and angiotensin-converting enzyme (ACE) inhibitor therapy intiated. She received rituximab for PTLD, and her prednisone was tapered to 2.5 mg per day. Over the next month, her creatinine improved to 1.4 mg/dL and dialysis was discontinued.

The reported rate of recurrence of SRC in renal allografts is about 2-5%. Use of prednisone >15 mg/day has been reported to precipitate renal crisis in patients with scleroderma. Steroids inhibit prostacyclin production and increase ACE activity, both of which can augment the pre-existing reno-vascular injury in this disease. Therefore, high-dose corticosteroids should be used with caution in renal transplant recipients with diffuse scleroderma

PREVALENCE OF REDUCED KIDNEY FUNCTION AND ERYTHROPOIESIS-STIMULATING PROTEIN USE IN PATIENTS ADMITTED TO THE INTENSIVE CARE UNIT.

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Reduced kidney function (RKF) and anemia amongst patients admitted to the ICU can complicate patient care and potentially worsen clinical outcomes. This study was conducted to determine 1) the prevalence of RKF and anemia upon hospital admission in patients requiring an ICU stay, 2) selected clinical outcomes of patients with RKF and, 3) the utilization of erythropoiesis-stimulating proteins (ESPs) among patients in the ICU.

A retrospective review of data from 18,967 ICU patients admitted to 34 US hospitals (January 2001 to June 2005) was conducted. Data were provided through the Solucient® ACTracker® database. Inclusion criteria were ICU stay > 24 hrs, age ≥ 18 years, not on chronic dialysis, and a hemoglobin (Hb) and serum creatinine measurement within 3 days of hospital admission. RKF was defined as an estimated (e) GFR < 60 ml/min/1.73m^2 (MDRD equation); anemia was defined as Hb < 11.0 g/dL.

The prevalence of RKF on hospital admission was 42.0%. The mean (SD) eGFR for patients with RKF was 38.2 (14.9) ml/min/1.73m^2; their age was 72 (13) years and 45.9% were men. On admission, the mean (SD) Hb was 11.9 (2.4) g/dL for patients with RKF and 12.7 (2.3) g/dL for patients without RKF. The overall prevalence of anemia on admission was 27.9%; anemia was present in 34.9% of the patients with RKF versus 21.9% of patients without RKF. Patients with RKF were less likely to survive to discharge than those without RKF (OR 2.9, 95% CI 2.6, 3.2). ESPs were prescribed for 3.9% of ICU patients.

The prevalence of RKF in patients not on dialysis admitted to the ICU was over 40% on hospital admission, and anemia was present in more than one-third of these patients. The majority of ICU patients did not receive an ESP. RKF is a prevalent comorbidity in ICU patients and is associated with a higher prevalence of anemia and worse outcomes.

METABOLIC CONTROL AND SOLUTE CLEARANCE USING COMMERCIALLY AVAILABLE SOLUTIONS IN CVVHDF.

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CVVHDF is being increasingly used in critically ill patients with acute renal failure. The CVVHDF protocol should provide optimal metabolic control and solute clearance. At the same time the protocol should be simple for implementation. In the current study, we investigated the use of commercially available solutions for CVVHDF. Data was collected in 29 patients with acute renal failure undergoing CVVHDF using Prismasate (Gambro, USA) and ACD-A solution.

All patients received CVVHDF using the Prisma M 100 set with AN69 dialyzer. The mean age of the patients was 57±11 years (range 34-76). Prismasate BGK2/0 or BGK 4/0 was delivered as replacement fluid at 1500 ml/hr and Prismasate BGK4/2.5 was delivered as dialysate at 500 ml/hr. Calcium Chloride was administered as continuous intravenous infusion through central venous catheter to maintain iCa between 4.0 -4.5 mg/dl. Anticoagulant Citrate Dextrose – Formula A (ACD-A) was initiated at 150 ml/hr. The rate was adjusted to maintain post filter ionized Calcium between 1-1.4 mg/dl. Data (mean±SD) are summarized below.

Variable	0 hour	48 hours	96 hours	P value
Sodium	139.5±6.3	139.5±4.0	139.3±3.4	NS
Potassium	4.71±0.97	4.07±0.48	4.15±0.56	<0.01
Chloride	104.06±8.9	100.96±5.7	101.76±5.4	<0.05
Bicarbonate	22.03±5.40	26.13±4.53	27.76±5.26	<0.001
Anion gap	13.37±8.5	12.34±7.2	9.81±9.5	NS
PH	7.30±0.09	7.40±0.09	7.40±0.09	<0.001
BUN	63.62±25.74	43.27±19.15	41.69+22.80	<0.001
Creatinine	3.85±1.84	2.50±1.29	2.0±1.14	<0.001
Serum citrate	_	3.82±1.98	3.68±1.92	NS

The use of commercially available solutions is simple and provides adequate metabolic control and solute clearance in CVVHDF.

DEVELOPMENT OF AN ACUTE TUBULAR NECROSIS CAST SCORING INDEX: A PILOT STUDY

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Urine microscopy is a valuable tool when making a diagnosis of acute tubular necrosis (ATN), however, the manner in which nephrologists prepare, examine, and report urinary sediment findings is quite variable. The presence of granular and renal tubular epithelial (RTE) casts on urinalysis is known to be helpful in making a diagnosis of ATN, but a simple system to score the amount of casts is lacking. We developed an ATN Cast Scoring Index (CSI) as a framework to grade the degree of granular and RTE casts found on urinalysis. Further, we sought to assess the precision of this scoring system.

Urine samples from 30 patients with the clinical syndrome of ATN were collected at the George Washington University Hospital in Washington, DC. Sample preparation was uniform, and based on a combination of recommendations from various nationwide acute kidney injury (AKI) experts. A panel of 3 blinded nephrologists was instructed to view and grade each slide using the ATN CSI. Grade 0 refers to no evidence of granular or RTE casts, while grade 1 signifies rare granular or RTE casts (at least one seen on the entire slide, but less than 10% of low power fields), grade 2 refers to a moderate amount of casts (many granular or RTE casts, but not seen on every low power field), and grade 3 signifies sheets of muddy brown casts (granular or RTE casts seen in 100% of low power fields).

The scores of the three reviewers completely matched for 14 of 30 slides (46.7%), and all three reviewers agreed within one grade in 29 of 30 instances (96.7%). Intercorrelation coefficient was 0.787.

We conclude that the ATN CSI is a simple, novel, reliable scoring system to grade the degree of granular and RTE casts present on urine microscopy. A standardized ATN CSI has the potential to incorporate urinary cast analysis into the advancing field of AKI diagnostics.

DIAGNOSIS OF ETHYLENE GLYCOL POISIONING BY URINALYSIS; A CASE OF MISTAKEN IDENTITY

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Patients with ethylene glycol intoxication typically present with a high anion-gap metabolic acidosis, renal failure, and a high osmolar gap. In cases where a clinical history is unavailable, examining the urinary sediment can be extremely useful. Typically the urine sediment will contain calcium oxalate crystals, classically in the envelope shaped dihydrate form.

Case Report: A 40 year old female was found unresponsive in the back seat of her car, beside an open bottle of antifreeze. In the emergency department, she was comatose, was intubated, and labs revealed an anion gap metabolic acidosis and renal failure. There was no osmolar gap. The urine was initially reported to have numerous hippurate crystals, and no calcium oxalate crystals. An ethanol infusion was started, and she was dialyzed until her anion gap was normal. Her admission serum ethylene glycol level was later found to be zero, but after waking up, she admitted to ingesting an unknown amount of antifreeze. She received intermittent hemodialysis for another week, and her renal function slowly improved to normal.

Discussion: The initial report of only hippurate crystals in the urine was misleading, but fortunately did not delay therapy for suspected ingestion. After ethylene glycol ingestion, the envelope- shaped crystals predominate initially. Over the next several hours these crystals are replaced by the needle-shaped monohydrate crystals. These needle-shaped crystals resemble hippurate, and may be mistaken for such. Additionally, the failure to find ethylene glycol in this patient's blood was misleading. The half-life of ethylene glycol in humans has been reported to be 3-8 hours, so it was fully metabolized by the time that this patient came to medical attention. The absence of ethylene glycol explains the normal osmolar gap.

We bring this case to the attention of practitioners to illustrate the features of ethylene glycol poisoning with delayed presentation and to point out that ethylene glycol crystalluria can be mistaken for hippurate crystalluria in this setting.

ELEVATED VANCOMYCIN LEVELS AS A RESULT OF ORAL AND INTRACOLONIC VANCOMYCIN IN A PATIENT WITH RENAL FAILURE.

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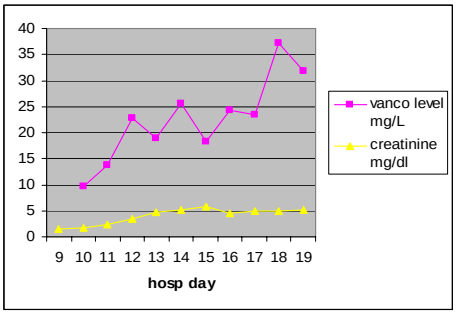
Oral vancomycin is widely used as therapy for Clostridium Difficile (C.diff) colitis, and vancomycin enemas have also been reported to be helpful in these cases. Systemic absorption of oral vancomyin has been reported to be minimal, even in those with renal insuficiency. We report on a case of toxic serum levels of vancomycin in a patient receiving oral and intracolonic vancomycin with acute renal failure and severe colitis.

The patient was a 76 year old male with diabetes and coronary artery disease admitted with pneumonia and myocardial infarction. He was started on intravenous moxifloxacin. On hospital day (HD) 9, severe diarrhea developed. Assay for C. diff toxin was positive. The patient was given 2 doses of intravenous vancomycin as well as oral vancomycin at 250 mg every six hours. The patient's renal function worsened, requiring dialysis on hospital day 15. Severe colitis was diagnosed, and vancomycin enemas were instituted on HD 14. The vancomycin levels continued to rise despite receiving no further IV doses and peaked at 37.2 mg/l on HD 18.



There have been few reports of elevated serum vancomycin levels with enteral therapy in the literature, but there currently is no recommendation to follow levels of the antibiotic. We describe a complicated case where serum concentrations reached toxic levels. We feel it is prudent to monitor the levels of vancomycin in cases of Clostridium Difficile complicated by renal failure and severe colitis.

PROVIDER UNDERSTANDING OF THE RISK FACTORS AND PREVENTIVE INTERVENTIONS FOR CONTRAST-INDUCED NEPHROPATHY (CIN)

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Little is known about medical providers' understanding of the risk factors and preventive strategies for CIN. We sought to assess provider understanding of the risk factors and preventive measures for CIN.

We identified all providers caring for patients at high risk for CIN who were undergoing procedures using radiocontrast at a single VA medical center. Providers completed a 22-item survey to assess their: i.) experience with and prior training on CIN; ii.) knowledge of the risk factors and preventive interventions for CIN; and iii.) personal practice for the prevention of CIN.

Overall, 89 providers completed the survey. Fifty-seven providers (64%) reported receiving little or no prior training on CIN. Chronic kidney disease and intravascular volume depletion were correctly identified by 96% of providers as risk factors. Conversely, 36 providers (40%) incorrectly reported allergy to radiocontrast as a risk factor. Thirty-six providers (40%) correctly reported that intravascular isotonic NaCl and NaHCO3 prevent CIN, 52 (59%) described that limiting the volume of radiocontrast media was protective, and 50 (57%) identified low or iso-osmolar radiocontrast as least nephrotoxic. Just over half (52%) of providers indicated that N-acetylcysteine had been conclusively shown to prevent CIN, while 3.4% reported diuretics and 5.6 % described fenoldopam as protective. Seventy-five providers (84.2%) reported using isotonic saline and 45 (51%) described administering isotonic sodium bicarbonate on a regular basis. However, 5% confirmed that they administered intravenous diuretics to prevent CIN and one provider acknowledged using calcium channel blockers as a preventive agent. Only 24.7% agreed that the level of renal impairment at which risk of CIN rises depends on patients' gender, age, and race along with serum creatinine concentration.

Consistent with the limited training providers receive on CIN, there is significant variation in understanding of the risk factors and preventive strategies. A small but significant proportion of providers report using agents that have been shown to be ineffective. Efforts to disseminate research findings on CIN to the broader medical community are essential to improve provider understanding of this condition and to reduce the incidence of this costly iatrogenic condition.

ACUTE KIDNEY INJURY IN A PATIENT WITH MASSIVE ASCITES AND INCREASED INTRA-ABDOMINAL PRESSURE

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Acute Kidney Injury (AKI) in the setting of liver failure and ascites is often thought to be secondary to either pre-renal azotemia, ATN, or hepatorenal syndrome. The hemodynamics of increased intra-abdominal pressure (IAP) and abdominal compartment syndrome have gained significant attention in the trauma and critical care literature. A MEDLINE search yielded only a few cases involving IAP in patients with liver failure and massive ascites.

We report the case of an 82-year-old male, with a past medical history of cirrhosis and recurrent ascites, admitted to the ICU due to acute respiratory distress and anuria. The patient had AKI: Labs showed a BUN of 77 mg/dl, creatinine of 4.4 mg/dl, and K of 7.5meq/l.

The abdominal exam demonstrated massive ascites, which was confirmed by ultrasound. Intravesicular bladder pressure was 32 mmHg. Paracentesis was performed, and 10 liters of fluid was drained. The patient was started on hemodialysis. Within 24 hours of paracentesis his kidney function had drastically improved, with a significant increase in urine output. Dialysis was discontinued and a Tenckhoff catheter was placed in the abdominal cavity for ascites drainage.

Many mechanisms have been proposed to explain the effects of IAP on renal function. An IAP above 30 mm Hg is related to significant anuria. Renal derangements involve a reduction in effective renal blood flow, corticomedullary shunting of renal plasma flow, reduction of GFR, water reabsorbtion, and increasing renal venous pressure. We believe that IAP with altered renal hemodynamics should be considered in the differential diagnosis of AKI in a patient with cirrhosis and ascites, especially in those patients with tense ascites.

ROLE OF SODIUM BI CARBONATE IN PREVENTING CONTRAST INDUCED ACUTE KIDNEY INJURY

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PURPOSE: The purpose of our study was primarily to assess the role of intravenous hydration fluids in prevention of contrast induced acute kidney injury.

METHODS: We reviewed 105 charts and obtained information on demographics, medical history, medications and laboratory data. Out of these, 77 patients received prophylaxis with Normal Saline and 28 patients with sodium Bicarbonate prior to the contrast study. Some patients received Mucomyst in addition to hydration. We evaluated for differences in percentage change in the mean value of creatinine levels after contrast exposure in the 2 groups. The primary statistical analysis was Analysis of Variance. A p-value less than 0.05 the result was considered statistically significant.

RESULTS: Patients with congestive heart failure (CHF) ($p=0.003$) and Hypertension ($p=0.027$) were at higher risk for increase in creatinine after a contrast study. Patients not on Calcium channel antagonists had better outcome ($P=0.056$). A protective effect was noted for individuals who were on β-blocker or Statins; diabetes (DM) had worse outcome. However, these associations were not statistically significant.

Patients with CHF or history of CHF had better outcomes if they received Bicarbonate. Also, patients with chronic kidney disease and DM on Bicarbonate had better outcome.

CONCLUSIONS: Sodium Bicarbonate has a favorable effect in preventing contrast induced acute kidney injury in patients with comorbidities.

CLINICAL IMPLICATIONS: Patients should be assessed for different comorbidities prior to contrast studies and prophylaxis with Bicarbonate must be considered.

EVALUATION OF THE UAB 0.5% CITRATE CVVHDF PROTOCOL WITH PRISMAFLEX

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We previously described an effective simple regional citrate protocol for continuous veno-venous hemodiafiltration (CVVHDF) with the Prisma using 0.5% Trisodium Citrate (TSC) as pre-filter replacement fluid (RF) and Prismasate as dialysate. We performed a prospective analysis of the first 72 hours of therapy for 7 ICU patients on the Prismaflex using our 0.5% TSC protocol. Since our 0.5% TSC solution doubles as an anticoagulant and RF, we infused it in the pre-blood pump port of the Prismaflex and did not use the RF pump. Patient demographics, CVVHDF parameters, and metabolic status were recorded daily. Nursing staff were asked to record reasons for set changes and any technical problems during this trial.

43% patients were female; the mean age was 52.4 yrs, weight 85.0 kg, and APACHE II score 25. The mean pre-blood pump 0.5% TSC rate was 1448 ml/hr, dialysate rate 1754 ml/hr, BFR 142 ml/min, and mean effluent rate of 43 ml/kg/hr. Post-filter ionized calcium levels were in therapeutic range. Kaplan-Meier survival curve demonstrated 60% dialyzer patency at 72 hours. Reasons for set changes included 2 episodes from clotting in the aeration chamber and 3 episodes due to very negative access pressures.

Our UAB 0.5% TSC protocol can be successfully used with the Prismaflex. However, clotting in the aeration chamber may be problematic if the RF pump is not used.

SEVERE NEPHROTIC RANGE PROTEINURIA IN A PRIMIGRAVID WOMAN OF 22 WEEKS GESTATION

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Preeclampsia is a multiorgan disease typified by the presence of an abnormal placenta and the presence of systemic endothelial dysfunction and microangiopathy. Severe proteinuria has been associated with worse outcomes, and so definitive diagnosis may be desired in such cases to guide treatment and predict outcomes.

A 31-year-old woman presented with hypertension and proteinuria at 22 weeks of pregnancy. She had no prior pregnancies, no previous medical history and no documented hypertension. She was acting as a surrogate for her sister. Fetal demise of one twin occurred at 6 weeks. Prenatal course was otherwise unremarkable and her only medications as an outpatient were prenatal vitamins. She was initially admitted due to worsening proteinuria (18 gm/24hr) and rising blood pressure (164/99 mm Hg). Further family history at this time revealed that the patient's mother had an erythematous facial rash during pregnancy that resolved after delivery. Over the course of the admission, proteinuria worsened and creatinine rose to 1.5 mg/dL. Proteinuria persisted with a peak up to 27 gm/24hr.

Cases consistent with preeclampsia do not necessarily exclude an underlying renal disease. The patient had a low C4, positive ANA, and family history of the mother's rash that could also be indicative of early lupus. In addition, the severity of proteinuria led to concern for an underlying renal disease.

Percutaneous renal biopsy was performed under ultrasound guidance at 24 weeks and showed endotheliosis, glomerular capillary occlusion, a full house of immunoglobulin deposits and subendothelial electron dense deposits - signs of both preclampsia and early lupus nephritis.

Although the patient's course was consistent with preeclampsia, the biopsy was felt to be indicated based on the severity of her proteinuria and clinical course. After delivery, the patient's blood pressure returned to 120/80 and she remained normotensive at follow up visits. Most of her lab results began to normalize as well although urine protein remained elevated at 2 gm/24hr and her ANA titer peaked to 1:640 hinting at the remaining possibility for lupus.

LOWER MORTALITY IN ACUTE KIDNEY INJURY (AKI) WITH INTERMITTENT HEMODIALYSIS (IHD) WHEN COMPARED WITH CONTINUOUS RENAL REPLACEMENT THERAPY (CRRT) AND SLOW LOW EFFICIENCY DIALYSIS (SLED): A SYSTEMATIC REVIEW AND META-ANALYSIS

Anis Abdul Rauf, Judith A. Beto, Vinod K. Bansal

Acute kidney injury (AKI) is associated with a high mortality. Currently there is no consensus with regard to definition, dose and optimum dialysis modality to treat AKI in the intensive care unit (ICU). Renal replacement therapy (RRT) is limited to forms of intermittent hemodialysis (IHD), continuous renal replacement therapy (CRRT) and IHD/CRRT hybrid therapies such as slow low efficiency dialysis (SLED). The literature has failed to show a survival difference between these modalities.

We systematically collected all published reports that studied these different dialysis modalities from 1985 to 2006. We used strict inclusion-exclusion criteria to systemically review and analyze results between these different modalities using meta-analysis techniques.

Our meta-analysis is consistent with other studies that suggest a high mortality in AKI. IHD showed a statistically significant improvement in mortality by 4.84% non-overlap effect.

Modality	Data	Crude Mortality	Random Effects Adjusted Combined Model With 95% Confidence Interval	Effect Range with 95% Confidence Interval (CI)
CRRT	1164 patients 15 studies	62.63%	64.80% ± 2.63%	62.17-67.43%
IHD	1157 patients 15 studies	54.45%	54.54% ± 2.79%	51.75-57.33%
SLED	141 patients 6 studies	58.87%	62.09% ± 7.58%	54.51-69.67%

A slight reduction in mortality was seen in AKI patients treated with IHD as compared with others. There is an obvious need for a more uniform approach towards the treatment of AKI. Additional comparative studies are warranted to confirm the strength of these findings.

STUDY TO COMPARE EFFECT OF DIFFERENT MODALITIES OF ACUTE DECOMPENSATED HEART FAILURE TREATMENT ON RENAL FUNCTION, Syed Saghir, Farhan Arif, Michael Cardi, The Christ Hospital, Cincinnati, Ohio

In acute decompensated heart failure (ADHF), the standard of care is based on loop diuretics. Nesiritide (N) is an adjunctive therapy used to rapidly improve symptoms and promote naturiuresis, while ultrafiltration (UF) is an effective way to remove fluid in diuretic resistance. We compared usual care (UC), UF, and UC plus N in a case control study to evaluate the effect on renal function.

Twenty five HF inpatients that underwent UF were selected based on completeness of clinical data. UC and N groups were matched for age, gender, ejection fraction, etiology of HF, and creatinine. The decision to use UF, N or UC was a clinical decision for the attending cardiologist. Mean UF rate was 325 ±117 (ml/hr), with a mean duration of 38 ±25 (hrs). Diuretics were held during UF but not during N infusion. Data were collected by chart review. There were no significant differences in patient demographics, co-morbidities or baseline laboratory values. Results are shown below.

	UC (n = 25)		UF (n = 25)		N (n = 25)	
	Pre-Rx	Post-Rx	Pre-Rx	Post-Rx	Pre-Rx	Post-Rx
Hematocrit (%)	36.7 ± 7.2	35.9 ± 6.2	34.0 ± 4.8	34.2 ± 5.5	38.1 ± 7.9	35.4 ± 6.2
Sodium (mg/dl)	138.4 ± 3.0	137.5 ± 2.5	135.3 ± 6.5	133.7 ± 6.9	136.0 ± 4.7	136.5 ± 4.0
BUN (mg/dl)	34.6 ± 23.5	38.8 ± 26.0	51.6 ± 28.8	61.2 ± 34.7*	35.9 ± 19.3	37.2 ± 21.8
Creatinine(mg/dl)	1.8 ± 0.8	1.9±1.0	1.9±0.8	2.2±1.1*	1.5±0.6	1.5 ± 0.7
Weight (lbs)	223.1 ± 75.7	216.8 ± 74.3*	229.7 ± 73.3	213.8 ± 68.1*	205.6 ± 74.1	201.0 ± 76.6
Weight Δ (lbs)	6.3 ± 7.6		15.8 ± 13.6		4.7 ± 10.9	
± standard deviation, * $p<0.01$ vs. pre-treatment value						

In conclusion, among patients with ADHF, UF appears to be a more effective method to remove volume, and relieve symptoms than UC or UC plus N, but with relatively greater increase in BUN and creatinine.

LISTERINE-INDUCED ACUTE RENAL FAILURE

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INTRODUCTION: Massive mouthwash ingestion is a rare occurrence. Severe complications, such as acute renal failure, multi organ dysfunction and cardiac arrest can occur after massive mouthwash ingestion. It is still unclear which of the components of this product is responsible for the complications. Phenol compounds (menthol, eucalyptol and thymol) may be playing an important role.

Case: A 38-year-old homeless male from Brazil, with history of alcohol abuse and chronic obstructive pulmonary disease, was brought to the emergency department in an intoxicated state. The patients labs on admission were as follows: BUN 15 mg/dL, creatinine 2.5 mg/dL and potassium 8.3 mEq/L, with tall, peaked T waves on electrocardiogram. Plasma pH was 7.05, serum bicarbonate 3 mEq/L, and anin gap 33. The measured serum osmolality was 312 mOsm/KgH2O, with an osmolal gap of 21. Lactic acid level was 80 mg/dL, and serum levels of ethanol, salicylates and paracetamol were undetectable. Urinalysis was positive for calcium oxalate crystals. Fomepizole and emergent hemodialysis were initiated for suspected ethylene glycol intoxication. The patients mental status improved, but remained anuric and the elevation of creatinine to 9 mg/dL. The patient later admitted to drinking an entire bottle of Listerine® (1 liter), but denied any ethylene glycol or methanol ingestion.

Daily hemodialysis (HD) was required for the first few weeks; however, over the course of the 2nd and 3rd weeks the urine output progressively increased. The patient was discharged with a stable serum creatinine (4.7mg/dl).

CONCLUSION: Mouthwash ingestion leading to severe renal failure is rare yet not uncommon. Kidneys may be the first organ to get affected based on clinical presentation of our patient. Ethanol was incriminated in previous reports as the main agent responsible for the organ failure and metabolic disturbances. However, ethanol constitutes only 27% of the preparation, and it is very likely that phenol compounds play a major role in the pathogenesis of the poisoning.

USE OF HIGH-FLOW CONTINUOUS VENO-VENOUS HEMOFILTRATION WITH CITRATE ANTICOAGULATION AND MAINTAINING HYPERNATREMIA IN A PATIENT WITH ACUTE BRAIN INJURY

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The use of high flow continuous renal replacement therapy (CRRT) for renal replacement therapy in acute kidney injury has grown in popularity. Citrate anticoagulation in CRRT has also grown in popularity given its remarkable success as a regional anticoagulant. However, utilizing citrate anticoagulation with continuous veno-venous hemofiltration (CVVH) has been less frequently described. Concerns about electrolyte abnormalities including hypernatremia have limited its use. There are increasing reports of inducing hypernatremia in the context of traumatic brain injury to acutely lower elevated intracranial pressure. We describe an otherwise healthy 18 year old man who presented with traumatic brain injury whose case was complicated with persistently elevated intracranial pressures, acute respiratory distress syndrome, and acute kidney injury. CVVH was implemented utilizing regional citrate anticoagulation. Accounting for the sodium load from the trisodium citrate, the replacement fluid was adjusted to maintain hypernatremia. Within days of CVVH initiation the patient's ICP improved, hemodynamics improved, and respiratory status also improved. The serum sodium was maintained at goal and furthermore there were no episodes of alkalosis due to the citrate metabolism. We report the first case of CVVH induced hypernatremia successfully used in acute kidney injury specifically for the correction of elevated ICP following acute traumatic brain injury.

SIMULTANEOUS DEVELOPMENT OF FANCONI SYNDROME AND ACUTE TUBULAR NECROSIS (ATN) AFTER ADMINISTRATION OF CIDOFOVIR mohammed singapuri, ormc, orlando, fl, usa, anuradha wadhwa, amir kazory, a.a. ejaz, uf shands, gainesville, fl, usa.

Cidofovir is an antiviral nucleotide analogue with significant activity against almost all types of DNA viruses including adenovirus. Nephrotoxicity is one of the adverse effects of cidofovir, which seems to be dose-dependent & partially reversible after cessation. Here, we present a second case of cidofovir-related nephrotoxicity extending from ATN to Fanconi syndrome, which to our knowledge, there is only one reported case of this association in the medical literature.

A 34 year old Hispanic male with chronic myelogenous leukemia received an umbilical cord transplant in May 2006. Post-transplant course was complicated by adenoviremia as well as BK virus-related hemorrhagic cystitis for which patient received 1mg/kg of Cidofovir three times a week. He was hydrated with normal saline and received probenecid 2 grams PO 3 hours prior to Cidfovir infusion and 2 grams PO 2 and 8 hours after the infusion. Renal function was normal with a serum creatinine (Cr) level of 0.7mg/dL. Three weeks after initiation of treatment, he developed acute kidney dysfunction with a Cr rising to 1.4mg/dl necessitating cessation of Cidofovir. Ten days later, the plasma adenovirus load rose to 16,000 and Cidofovir was restarted. His kidney function again deteriorated rapidly and serum Cr, which was stabilized around 1.6mg/dL, increased to 3.0mg/dl with normal urine output. At this time, laboratory studies showed serum BUN 20mg/dl, Na 140mg/dl, HCO3 10mmol/l, Cl 121mmol/l, Mg 1.3mg/dl, PO4 2.4mg/dl and glucose of 78mg/dl. Urine analysis revealed glycosuria (>1000mg/dl), proteinuria (100mg/dl), hyperphosphaturia (18.7mg/dl) and hypermagnesuria (143mg/dl) with no eosionophils. Renal ultrasound was normal and microscopic exam of the urine revealed multiple granular casts compatible with ATN. Conservative management, including repletion of K, Mg, PO4, and HCO3 as well as discontinuation of Cidofovir was followed by correction of electrolyte abnormalities and gradual improvement in kidney function. At the time of discharge serum Cr level had decreased to 1.6 mg/dl and electrolytes were within normal range.

ACUTE PHOSPHATE NEPHROPATHY (APN): AN UNAPPRECIATED ETIOLOGY OF ACUTE KIDNEY INJURY

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Many patients are subjected to phosphate-based enemas in preparation for GI procedures, including colonoscopy. In patients with pre-existing CKD, the deposition of calcium and phosphate within the kidney tubule is an unappreciated etiology of acute kidney injury (AKI). We present the case of a patient with CKD who was found to have this as an etiology of AKI on renal biopsy.

A 74-year-old female with a baseline creatinine of 1.5 mg/dl presented with a creatinine of 3.4 mg/dl. Her past medical history consisted of atrial fibrillation. HTN, CAD, MI. Six months prior to this presentation she had undergone a colonoscopy following the use of a phosphate-based bowel preparation. A renal biopsy demonstrated multifocal distal tubular calcification consistent with nephrocalcinosis. There was also accompanying mild tubular atrophy and interstitial fibrosis and moderate arteriosclerosis.

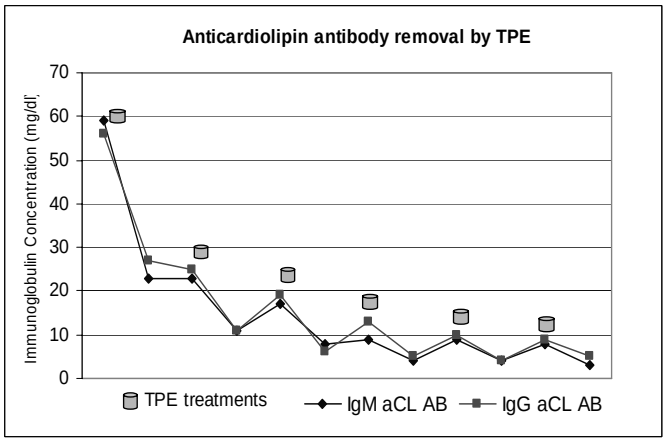
Various case series have described risk factors for APN, many of which were applicable in our patient: advanced age, a history of hypertension and the use of ACE or ARB (our patient was on Cozaar). She may have been pre-renal at the time of the procedure.

We feel that use of a phosphate-based bowel preparation is an unrecognized etiology of AKI. A question about enema use should be included in the evaluation of any patient with AKI or CKD. It may also be prudent to consider withholding the use of ACE inhibitors, diuretics, ARBs, and/or NSAIDS 48 hours before a procedure if an enema preparation is to be used. Finally, an estimate of a steady state creatinine by MDRD should be calculated before such a procedure to better stratify a person's risk of acquiring AKI.

PREDICTABLE REMOVAL OF ANTICARDIOLIPIN ANTIBODY (aCL AB) BY THERAPEUTIC PLASMA EXCHANGE (TPE) IN A PATIENT WITH CATASTROPHIC ANTIPHOSPHOLIPID ANTIBODY SYNDROME (CAPS) Tausif Zar, Atiq Dada and Andre A. Kaplan. University of Connecticut, Farmington, CT, USA

CAPS is a rare, life-threatening condition. Treatment consists of heparin, steroids, IVIG and/or TPE. We report predictive and effective removal of pathological aCL AB using TPE. A 33 yr old female with history of antiphospholipid antibody syndrome presents with CAPS (hemiplegia, MI and ARF). She is started on above management including TPE. She received 2 treatments of TPE on the 1st day, twelve hours apart and then daily for 4 days, using 3 liters of albumin and 1 liter of FFP. Patient completely recovered. Decline in immunoglobulin level after a single TPE can be predicted with first order kinetics by calculating the ratio of Volume exchanged (Ve)/ Expected Plasma Volume (EPV). Similar to the KT/V prescription for urea reduction, Ve/EPV ratios of 0.7, 1.0 and 1.4 are expected to yield a 50%, 63% and 75% decline in immunoglobulin level respectively. In the above case Ve/EPV was 1.0 and predicted decline would be 63%. The achieved average daily decline in aCL IgM and IgG levels was 57 % & 59 % respectively.

CCL: As with KT/V for urea reduction, removal of aCL AB by TPE follows first order kinetics and can be accurately predicted.



FACTORS ASSOCIATED WITH MICROALBUMINURIA IN RESISTANT HYPERTENSIVE TYPE 2 DIABETICS UNDERGOING SCREENING FOR PRIMARY HYPERALDOSTERONISM

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Background: Microalbuminuria (MA) and HTN are associated with diabetic nephropathy. In addition, MA is independently associated with greater cardiovascular risk. We evaluated predictors for MA in resistant HTN (defined as BP > 140/90 mmHg in spite of ≥3 antihypertensive agents) in patients with type 2 diabetes.

Methods: 64 (40 women and 24 men) DM patients with resistant HTN, serum creatinine <1.4mg/dL, had albuminuria determined in a morning void. MA was determined from the ratio of urinary albumin:creatinine. We assessed distribution of MA in our study population by age, BMI, DM and HTN duration. Other variables including LDL cholesterol, Hgb A_1C, plasma aldosterone (PAC) concentration, plasma renin activity (PRA) and PAC/PRA were also measured. MA was diagnosed with a ratio of urinary albumin to creatinine excretion of 30 to 300 mg/g creatinine.

Results: MA was present in 38% of both men and women. MA correlated with LDL cholesterol and HTN duration (95% confidence interval, 1.008 to 1.052 for LDL and 0.9 to 1.0 for HTN. $p<0.05$). Patient's age (mean 60 years), duration of DM (mean 7.8 years), HgA1C (mean 7.85%), PAC (mean 11.4 ng/dL) and PAC/PRA ratio (mean 37.7 ng/dl/ng·ml^{-1}·h^{-1}) did not predict MA.

Conclusions: Microalbuminuria is present in a >35% type 2 diabetic patients with resistant HTN. PAC and PAC/PRA are not related to the presence of MA. However, traditional cardiovascular risk factors including HTN and LDL cholesterol are related to MA.

RENAL OUTCOMES IN METFORMIN USERS VERSUS NON-METFORMIN USERS IN VETERANS WITH TYPE 2 DIABETES MELLITUS (T2DM). E. Gosmanova[2], R.B. Canada[2], T.A. Mangold[1], W.N. Rawls[1], and B.M. Wall[1,2]. [1]VAMC, Memphis, TN. [2]UTHCS, Memphis, TN.

Little is known if any particular anti-diabetic drug or regimen is superior for renal outcomes. The aim of this study was to examine the relationship between metformin use and a decline in renal function in veterans with T2 DM. We studied a cohort of 1,493 veterans treated for T2 DM at the VAMC using computerized medical records in the calendar year 2000. All patients had baseline serum creatinine concentration (SCr) $\leq$ 1.5mg/dL. A decline in renal function, defined as 0.5mg/dl increase in SCr, was compared among cohorts of metformin users (n-812) versus non-metformin users (n-681) on an intention to treat basis. Cox regression analysis was used to estimate the hazard ratio (HR) for the decline in renal function after adjusting for age, race, insulin use, use of ACEI/ARBs or statins, estimated GFR (eGFR), HbA1C and level of baseline albuminuria. Normal albuminuria was defined as urinary albumin excretion as < 50mg/L, microalbuminuria as 50-299 mg/L, and macroalbuminuria as > 300 mg/L.

The average length of follow up in metformin and non-metformin users was 55$\pm$13 and 57$\pm$14 months, respectively. Both groups were similar in age, race and exposure to ACEI/ARBs. Metformin users had higher baseline eGFR, albuminuria, HbA1C, and had higher exposure to insulin and statins. Among those using metformin, 133(16.4%) patients developed elevation of baseline SCr, compared with 83(12.2%) patients in non-metformin users (unadjusted HR 1.82, $p<0.001$). The presence of micro- and macroalbuminuria and exposure to insulin and ACEI/ARBs were independent predictors of decline in renal function. However, after adjusting for age, race, baseline eGFR, albuminuria, HbA1C, use of insulin, exposure to statins or ACEI/ARBs, metformin use remained a predictor of adverse renal outcome (adjusted HR 1.53 [95%CI 1.31-2.06], $p<0.006$).

In conclusion, treatment of T2 DM with metformin alone or in combination with other hypoglycemic agents was associated with more frequent declines in renal function, as compared with no metformin use. Additional research is needed to assess for other potential confounding factors before definitive conclusions concerning metformin use and adverse renal outcomes can be drawn.

COMPARISON OF DIABETICS AND NON-DIABETICS IN A MODERATE TO SEVERE CHRONIC KIDNEY DISEASE COHORT

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Diabetes accounted for 45% of incident end stage renal disease (ESRD) patients from 2000-2004. As a result of the increasing prevalence of diabetes, the incidence and prevalence of chronic kidney disease (CKD) and ESRD are expected to increase further in the next few decades. We compared diabetics and non-diabetics in a retrospective cohort (n=1325) derived from October 2005 to April 2006, with at least two eGFR values, maximum of < 60 ml/min/1.73m² within a period of 12 months (moderate to severe CKD i.e. National Kidney Foundation stages 3-5). Patients on dialysis or with a renal transplant were excluded. In the cohort 490 (37%) patients were diabetic with 97% of these male and 3% female. Diabetics when compared to non diabetics were younger (74 ± 8.9 vs. 76 ± 9.4 years), had lower eGFR (43.3 ± 10.7 vs. 46.4 ± 9.8 ml/min/1.73m²) and higher serum Cr (2 ± 1 vs. 1.8 ± 0.8 mg/dL), all at p<.001. Diabetics were at a more advanced stage of CKD than non diabetics (88% stage 3, 11% stage 4, 1% stage 5 vs. 93%, 6% and 1%, p<.05). When eGFR values were compared to values obtained in the prior 12 months it had declined more in diabetics than non-diabetics (2.3 ± 6.2 vs. 1.5 ± 5.8, ml/min/1.73m², p<.05). More diabetics had renal clinic visits (23% of the diabetic patients vs. 12% of non-diabetics, p<.001). Compared to non-diabetics, diabetics had more coronary artery disease (43% vs. 32%, p<.001), hypertension (89% vs. 79%, p<.001) and congestive heart failure (16% vs. 10%, p<.01) but not peripheral vascular disease or chronic obstructive pulmonary disease. In diabetics vs. non-diabetics, there was more use of angiotensin converting enzyme inhibitors (54% vs. 32%), angiotensin receptor blockers (17% vs. 9%) and statins (69% vs. 49%), all at p<.001. In comparison to non-diabetic chronic kidney disease (CKD), diabetic CKD is associated with more rapid decline in renal function and more cardiovascular disease, but more use of renal protective medications and more nephrology referrals, in our elderly cohort.

ELEVATED FIBROBLAST GROWTH FACTOR-23 IN A PATIENT WITH METASTATIC PROSTATE CANCER AND HYPOPHOSPHATEMIA

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Tumor-induced osteomalacia (TIO) is a paraneoplastic syndrome characterized by osteomalacia, renal phosphate wasting, and severe hypophosphatemia. While elevated levels of Fibroblast Growth Factor-23 (FGF-23), a known phosphatonin, have been documented in patients with TIO secondary to various tumors, an association with prostate cancer has not thus far been described. We present a case of TIO secondary to metastatic prostate cancer in the setting of an elevated FGF-23.

An 83 year old male with metastatic prostate adenocarcinoma was initially treated with androgen deprivation. After imaging revealed worsening osseous involvement, he was started on docetaxel and monthly pamidronate. Concomitant with his increasing tumor burden, his previously normal phosphorus decreased to a nadir of 0.8 mg/dL, accompanied by severe fatigue. Despite discontinuing his chemotherapy and pamidronate, as well as providing supplemental phosphorus, his phosphorus ranged from 1.4-1.7 mg/dL.

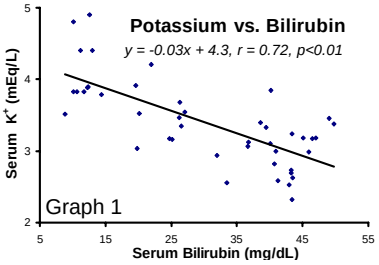
Additional evaluation revealed a creatinine of 0.8 mg/dL, an elevated fractional excretion of phosphorus of 21%, and a low renal phosphate threshold (TmP/GFR) of 1.25 mg/100ml with a normal 25-hydroxyvitamin D level and a low 1,25 dihydroxyvitamin D level. There was no evidence of fanconi syndrome, multiple myeloma, hyperparathyroidism, elevated parathyroid hormone related peptide, or diarrhea. An FGF-23 level was elevated at 326 RU/mL(normal 0-180).

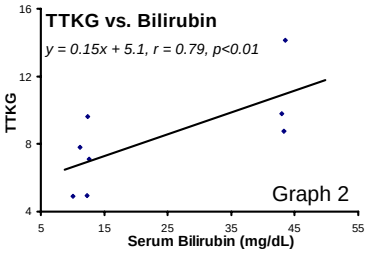
To our knowledge this is the first description of an elevated FGF-23 level in a patient with TIO secondary to metastatic prostate cancer. FGF-23 is a phosphaturic hormone that acts by decreasing proximal tubular phosphate reabsorption and by decreasing the synthesis of 1,25-dihydroxyvitamin D. Treatment of the disorder includes treating the underlying malignancy and supplementing the patient with phosphorus and calcitriol. Measurement of FGF-23 should be considered to support the diagnosis of TIO in patients with metastatic prostate cancer.

INTERMITTENT APPARENT MINERALOCORTICOID EXCESS IN A PATIENT WITH SICKLE CELL DISEASE

Manasvi Jaitly, Sumit Mohan, Geoffrey Moorer, Constance Park, Herman Anderson, Jen-Tse Cheng, Velvie Pogue. Harlem Hospital, Columbia University, New York, NY

A 23-year-old AA male with sickle cell disease presented with a hemolytic crisis. PE was significant for normotension, obesity, icterus, hepatomegaly and pitting edema. Pertinent labs: serum K^+ 2.8mEq/L, Mg^{2+} 1.9mg/dL, SCr 0.4mg/dL, TTKG 9, Hb 8gm/L, retic 10%, total bilirubin (TB) 40.7 mg/dL, ↓aldosterone 2ng/dL. After receiving exchange transfusions ↓K^+ resolved and TB ↓ to 9mg/dL. His serum K^+ remained normal until he was readmitted 3 months later with hemolytic crisis, ↓K^+ 3.1mEq/L, ↑TB 39mg/dL, TTKG 12. Evaluation of the ↓K^+ suggested renal K^+ wasting of an extra-adrenal origin and included the following: aldosterone 10ng/dL, ACTH 45pg/ml, cortisol 5.3µg/dL, 17-OH progesterone 25ng/dL (all normal), ↓DHEA 60 ng/dL and ↑bile acids (BA) levels 234µmol/L. ↑BA are known to inhibit 11β OH-steroid dehydrogenase (11βOHSD) activity thus preventing the renal conversion of cortisol to cortisone. ↑Tissue cortisol inappropriately activates mineralocorticoid receptors causing aldosterone independent Na^+ retention and K^+ wasting: the Apparent Mineralocorticoid Excess





syndrome (AME). We found a significant inverse correlation between the serum K^+ and TB (graph 1, r=0.72, *p<0.01)* and a significant correlation between the TTKG and TB (graph 2, r=0.79, *p<0.01*). We concluded that this patient's renal K+ wasting resulted from 11βOHSD inhibition by ↑BA and ↑TB. This is the first report of intermittent acquired AME associated with ↑BA and ↑TB levels resulting from hemolysis.

CONTRAST-INDUCED SEVERE HYPONATREMIA IN A PATIENT WITH NORMAL KIDNEY FUNCTION Ravi Makwana, Vinod Chacko, Binu Pappachen, Jay Krishnakurup, Mahesh Krishnamurthy, Arthur Levine. Easton Hospital/ Drexel University School of Medicine, Easton, PA, USA.

A strong correlation between the dose of contrast administered and change in sodium level is known in patients with advanced renal disease. However contrast induced hypertonic hyponatremia in a patient with normal renal function is uncommon, and severe hyponatremia is extremely rare. We report a case of contrast induced severe hyponatremia in a patient with normal renal function.

A 52-year-old man previously in good health presented with chest discomfort. He underwent cardiac catheterization for evaluation of these symptoms and was found to have multivessel coronary artery disease. He underwent a complicated and prolonged procedure with multiple coronary angioplasty stenting. A total of 2200 ml of intravenous dye was used during the procedure. After the procedure he was found to have marked electrolyte imbalances and acid base disturbance including serum sodium of 115 mEq/L, potassium 6.6 mEq/L, chloride 96 mEq/L and bicarbonate of 20 mEq/L. The BUN, creatinine and serum osmolality were reported to be 16, 1.3 and 328, respectively. On the morning before the procedure, the patient had had a BUN of 16, creatinine of 1.0, and normal electrolytes with serum sodium of 140 mEq/L, potassium 3.9 mEq/L, chloride 105 mEq/L and bicarbonate of 26 mEq/L. The patient reported no prior renal problems or voiding symptoms, and had no prior history of hypertension or diabetes. During the hospital course, he was treated with 0.9% normal saline and N-acetylcysteine. The sodium level normalized to 136 mEq/L within 24 hours and serum osmolality normalized to 284 within 72 hours. There were no neurological sequelae noted during the period of hyponatremia.

Our case suggests that a large volume of contrast may result in severe hyponatremia even in a patient with normal renal function. Serum electrolytes, especially sodium level, and renal functions should be closely monitored regardless of prior normal renal function when a patient receives a large volume of contrast.

REFORMULATED LANTHANUM CARBONATE: AN ANALYSIS OF EFFICACY AND SAFETY

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Poor adherence to phosphate-binder therapy in CKD Stage 5 patients due to high pill burden reduces likelihood of achieving KDOQI serum phosphorus targets (SP; 3.5–5.5 mg/dl). Lanthanum carbonate (LC), a non-calcium phosphate binder, has been reformulated in smaller tablets and higher strengths (500, 750, and 1000 mg) to reduce pill burden. The efficacy of reformulated LC was evaluated in a Phase IIIb multicenter clinical trial in patients undergoing maintenance hemodialysis.

Patients had a 0- to 3-week washout from previous binders, then began 3-part LC treatment: (1) 4-week open-label titration period (1500–3000 mg/day); (2) continuation in an open-label phase (1500–3000 mg/day) for patients reaching KDOQI SP target (cohort A) or a 4-week, double-blind, forced-dose (3000, 3750, or 4500 mg/day) titration for patients not at target after part 1 (cohort B); (3) a 16-week open-label extension for all patients.

A total of 513 patients (63% men; 36% white and 48% black) were enrolled. After 4 weeks, 54% of patients achieved the SP target range and entered cohort A (n=215). Mean change in SP for patients entering cohort A was –2.18 mg/dl from baseline ($P<0.0001$), and SP remained ≤5.5 mg/dl through week 24. Patients not reaching target SP at week 4 (cohort B; n=142) had dose-dependent SP changes by week 8 at doses of 3750 and 4500 mg/day; SP target was achieved in an additional 38% and 32% of these patients, respectively. There was no increase in the incidence or severity of adverse events with higher doses of LC. Mean corrected serum Ca, PTH (until week 24) and Ca × P product (after week 4) remained within KDOQI guidelines.

Most patients achieved SP control on ≤3000 mg/day LC. Higher doses (3750 or 4500 mg/day) of LC are well tolerated and may provide SP control for patients who do not respond to 3000 mg/day. Decrease in tablet burden with reformulated LC may help to improve patient adherence to phosphate-binder therapy.

EFFICACY OF DDAVP IN RAPID CORRECTION OF HYPONATREMIA

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To avoid iatrogenic complications, correction of chronic hyponatremia should be kept within therapeutic guidelines. However adherence to guidelines becomes difficult when a water diuresis emerges during therapy. Desmopressin acetate (DDAVP) has been used to end a water diuresis to avoid overcorrection of hyponatremia and to relower the serum sodium (SNa) following inadvertent overcorrection but experience is limited. We report our experience with this strategy in a 500 bed community teaching hospital.

Group 1: (n=10) were given DDAVP because of rapid increase in SNa by > 9 mmol/l in 24 hours; Group 2 (n=10) were given DDAVP for an anticipated overcorrection due to excessive urine output (median 267 ml/hr, IQR: 130, 331 ml/hr). In Group 1: presenting SNa was 114.2 ± 7.5 mmol/l, the increase in SNa before DDAVP was 13.5 ± 3.2 mmol/l and the rate of change of SNa from nadir to administration of DDAVP was 1.9 ± 1.4 mmol/l/hr; 60% had a relowering of SNa after the DDAVP. Correction was prevented from exceeding 18 mmol/l//48hours in 80%. In Group 2: presenting SNa was 115.3 ± 5.0 mmol/l, the increase in SNa before DDAVP was 4.9 ± 2.1 mmol/l and the rate of change of SNa from nadir to administration of DDAVP was 1.1 ± 0.8 mmol/l.hr; 40% had a relowering of SNa after DDAVP; correction was kept below 12 mmol/l/24 hrs in 90% and below 18 mmol/l/ 48 hrs in 100%; failure to prevent overcorrection was attributed to administration of repeat DDAVP doses at >12 hour intervals. No patients experienced post-therapeutic neurological complications.

In conclusion DDAVP can be used effectively to treat and prevent overcorrection of hyponatremia.

BEER POTOMANIA: A UNIQUE CAUSE OF HYPONATREMIA AT HIGH RISK OF COMPLICATIONS FROM RAPID CORRECTION

Shalin R. Sanghvi, Paul S. Kellerman, Lisa Nanovic
University of Wisconsin, Madison, WI, USA

Beer potomania is a unique syndrome of hyponatremia. Beer has low osmolality, and the caloric content prevents endogenous protein or ketone generation, leading to an excess of free water excretion limited by the low solute intake. These patients are at particular risk for rapid correction of their serum sodium after being challenged with solute. Thus, patients that present with beer potomania are at a higher risk of developing osmotic demyelination syndrome (ODS) due not only to the chronicity and degree of hyponatremia, but also due to the likelihood of rapid correction. We describe two cases of beer potomania with contrasting management strategies and different outcomes. The first case describes a 39 yo woman with severe hyponatremia (S Na = 100 mmol/L) whose rate of correction was 15 mmol/L in the first 24 hours and 24 mmol/L in the first 48 hours, who subsequently developed ODS. The second case is a 63 yo man presenting with severe hyponatremia (S Na = 104 mmol/L) whose rate of correction was 7 mmol/L in the first 24 hours and 14 mmol/L in the first 48 hours, and was later discharged home without neurologic sequelae. The major differences in management of these patients were the intravenous fluids received, the level of care, and the rapidity of serum sodium changes. Review of the literature reveals no evidence that aggressive correction of chronic hyponatremia improves prognosis. Furthermore, animal studies have shown benefit in relowering serum sodium to both decrease the likelihood of ODS and improve outcomes if there are neurologic signs or symptoms consistent with ODS. Based upon the literature and these two cases, an algorithm and management strategies are presented to treat hyponatremia from beer potomania including frequent serum sodium monitoring in the ICU and limiting the rise in serum sodium, with addition of free water infusion if needed. With proper identification of beer potomania, specific management goals, and judicious monitoring of serum sodium, the catastrophic outcome of ODS can better be prevented.

A RARE CASE OF DIABETES INSIPIDUS, PRE-ECLAMPSIA AND ACUTE FATTY LIVER IN PREGNANCY

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Background: Diabetes insipidus (DI) is a condition in which abnormal secretion; degradation or activity of vasopressin causes polyuria, polydipsia, and electrolyte abnormalities. Transient DI may rarely occur during late pregnancy or immediate puerperium, the prevalence being 1 in 300,000 pregnancies. If unrecognized, it may cause neurologic injury and threaten the lives of the mother and fetus. Case: A 19- year-old female patient (G3P1A1) at 28 weeks of gestation was admitted because of the risk of preterm delivery and suspicion of pre-eclampsia. It was a known gemellar (twin) pregnancy with suspected twin-twin transfusion. An ultrasound (USG) revealed a biophysical profile of 10/10 for both twins. She was given magnesium tocolysis to prevent pre-term labor. On the next day, she developed nausea, vomiting and frequent contractions. She was transferred to the labor and delivery unit. Labs were significant for proteinuria, hypernatremia and elevated liver enzymes. Subsequently, she became extremely thirsty and her urine output increased to 300 ml/hr with a very low specific gravity. Lab evaluation revealed high plasma osmolality (348mosm/kg), hypernatremia (168meq/l) and low urine osmolality (108mosm/kg). Repeat USG showed intra-uterine death of both the fetuses. She was subsequently induced. Treatment with desmopressin was initiated with improvement in patient's symptoms and lab parameters. Discussion: An increase in thirst threshold occurs in pregnancy due to reduced secretion and increased placental degradation of vasopressin by vasopressinase. In this patient, the gemellar nature of pregnancy could have induced excessive vasopressinase activity, and the hepatic dysfunction (acute fatty liver) could have reduced the catabolism of vasopressinase. Conclusion: Our patient had transient DI with subsequent fetal loss. We emphasize that pregnancies with transient DI should be considered at high risk because of association with pre-eclampsia and fatty liver.

FANCONI'S SYNDROME CAUSED BY CAPECITABINE, IRINOTECAN AND BEVACIZUMAB.

Aisha Shaikh and Nelson Leung, Mayo Clinic, Rochester, Rochester, Minnesota, Olmsted County

Fanconi's syndrome is a generalized dysfunction of the proximal tubules with no primary glomerular involvement. It is characterized by transport defect of glucose, phosphate, calcium, uric acid, amino acids, bicarbonate and other organic compounds. This syndrome can either be inherited or acquired. A number of anticancer drugs have been implicated to cause Fanconi's syndrome. We report a case of Fanconi's syndrome in a patient with metastatic colon cancer after treatment with capecitabine, irinotecan and bevacizumab.

A 77 year old female with metastatic colon cancer presented with vomiting and diarrhea. 5 days prior to admission she had finished her 11^{th} cycle of chemotherapy with capecitabine, irinotecan and bevacizumab. Her medications on admission included lisinopril, metoprolol, lovastatin, loperamide, prochlorperazine, ondansetron, pantoprazole, oxycodone and acetaminophen. She was found to have new onset hypocalcemia, hypophosphatemia, hypokalemia and hypouricemia. Urine glucose was 39 mg/dL of glucose in the presence of normal plasma glucose and 24 hour urine protein of 532 mg. Glucosuria and the presence of several electrolyte abnormalities suggested the possibility of Fanconi's syndrome. Fractional excretion of phosphorus was 91% (normal 5% - 20%). Neutral and basic aminoaciduria were noted on 24 hour urine collection. Urinary amino acids were: leucine 52 (normal 20-77 µmol/L/24 hr), phenylalanine 138 (normal 36-90 µmol/L/24 hr), serine 599 (normal 200-695 µmol/L/24 hr), lysine 433 (normal 32-290 µmol/L/24 hr), aspartic acid 69 (normal 14-89 µmol/L/24 hr) and glutamic acid 35 (normal 27-105 µmol/L/24 hr). Patient continued to have electrolyte abnormalities despite resolution of vomiting and diarrhea, and aggressive electrolyte replacement therapy. To the best of our knowledge, this is the first report of Fanconi's syndrome due to capecitabine, irinotecan and bevacizumab. It is unclear whether an individual drug or combination of these drugs is responsible but physicians need to be aware of this entity as the use of these drugs is becoming common.

SEVERE HYPOKALEMIA AND THYROID STORM SECONDARY TO IODINATED CONTRAST IN A HISPANIC MALE

Nandita Singh, Naheed Ansari, Anjali Acharya, Jacobi Medical Center, Bronx, New York, USA.

Thyrotoxic periodic paralysis (TPP) is a potentially lethal complication of hyperthyroidism affecting mainly males of Asian descent. It's clinical manifestations range from mild recurrent weakness to complete paralysis. The hallmark of this disease is hypokalemia with abnormal thyroid function tests. Hypokalemia is attributed to the massive shift of potassium into cells, increase in beta-adrenergic response and an increase in insulin sensitivity. We describe here a 20 year old Hispanic male with previously undiagnosed and asymptomatic hyperthyroidism presenting with alcohol intoxication and assault with head trauma. On presentation, patient had a left orbital fracture, BP of 131/66 mm Hg and pulse rate of 130 bpm. Labs on presentation showed serum potassium of 4.3 mEq/L with normal renal function. A CT scan of the orbits done with intravenous (IV) iodinated contrast agent showed multiple facial fractures with traumatic optic nerve damage. He was given IV Methyprednisolone and IV Acetazolamide for the optic nerve damage. Thyroid Function tests done 24 hours later due to tachycardia showed TSH of 0.007 U/L (0.47-6.9), T3 of 443.4 ng/dL (60-181ng/dl) and free T4 4.06 ng/dL (0.75-2.0ng/dl) consistent with the diagnosis of thyroid storm. A few hours later his serum potassium dropped to 1.2 mEq/L with EKG showing sinus tachycardia with widened QRS complex, QTc of 456ms and U waves. Patient was given 150mEq of potassium over the next 14 hours and was started on Propylthiouracil and intravenous Esmolol. Following this, the serum potassium level rose to 5.1mEq/L with normalization of the QRS complex and QT interval and resolution of U waves. Thyroid function tests run on the first serum sample prior to the CT scan showed a T4 of 6.08ng/dl and T3 level of >800 mg/dL. This is an unusual presentation of thyroid storm precipitated by IV iodinated contrast manifesting with severe hypokalemia in a patient with prior undiagnosed and asymptomatic hyperthyroidism. The patient's hypokalemia may have been exaggerated by administration of steroids and IV Acetazolamide. The patient did not show any signs of skeletal or respiratory muscle paralysis despite the severe hypokalemia.

CONVERSION TO LANTHANUM CARBONATE MONOTHERAPY MAINTAINS SERUM PHOSPHORUS CONTROL AND REDUCES TABLET BURDEN IN PATIENTS WITH CHRONIC KIDNEY DISEASE STAGE 5

Nirupama Vemuri, South Florida Nephrology Group PA, Coral Springs, FL, USA

Control of serum phosphorus (SP) is important for reducing morbidity in chronic kidney disease (CKD) Stage 5. Most oral phosphate binders require a high tablet burden that may diminish compliance. Lanthanum carbonate (LC) is an effective, non-calcium phosphate binder that is well tolerated by patients with CKD Stage 5. A large Phase 4 US study assessed the conversion from other phosphate binders (sevelamer and calcium-based binders) to LC monotherapy in a clinical practice setting.

After a 1-week observation period on previous binders, phosphate-binder therapy was changed (no washout) to LC for a 12-week titration period, followed by a 4-week LC maintenance period. SP, daily dose, and tablet burden were assessed at baseline and at weeks 12 and 16.

A total of 2763 patients were enrolled; 2643 patients (59% men; 49% diabetic; mean age, 56.4±14.3 yrs; median dialysis vintage 2.6 yrs) were in the safety population and 2520 comprised the intent-to-treat population. Patients previously maintained on a mean calcium-based binder dose of 5.4 g/day (n=1045) were titrated to mean LC doses of 2.7 and 2.6 g/day at weeks 12 and 16, respectively; mean SP was 6.01 mg/dl on calcium binders, 5.97 mg/dl at LC week 12, and 6.09 mg/dl at LC week 16. Patients maintained on a mean sevelamer dose of 7.6 g/day (n=958) were titrated to mean LC doses of 2.8 and 2.7 g/day at weeks 12 and 16, respectively; mean SP was 5.90 mg/dl on sevelamer, 5.86 mg/dl at LC week 12, and 5.94 mg/dl at LC week 16. At week 12, tablet burden was reduced by 35% and 28% for patients previously taking sevelamer and calcium-based binders, respectively ($P<0.001$ for both), with similar reductions at week 16.

In a clinical practice setting**,** conversion to LC monotherapy maintained SP with significant reductions in both daily dose and tablet burden. Effective LC doses for most patients were ≤3 g/day, which can be provided by one 1-g reformulated LC tablet with each meal, simplifying treatment and potentially improving patient compliance.

ASSOCIATION OF CHRONIC KIDNEY DISEASE (CKD) AND ANEMIA WITH HEALTH CARE SERVICES UTILIZATION

Marcus Alexander,[1] Sarita Mohanty,[2] Brian Bradbury,[3] Reshma Kewalramani,[3] Arie Barlev,[3] Denise Globe.[3] [1]Harvard University, Cambridge, MA; [2]Univ. of Southern California, Los Angeles, CA; [3]Amgen Inc., Thousand Oaks, CA

An estimated 18.9 million in the US have CKD stages I-IV. Despite the known link to adverse outcomes, little is known about the association of CKD and anemia with health care services utilization.

We estimated GFR and rates of persistent microalbuminuria using lab data collected from the Third National Health and Nutrition Examination Survey (1988-1994) to classify individuals according CKD stage. We assessed the association of CKD stages and anemia with health care utilization using survey-weighted regression based on self-reported hospitalization (Hosp) and physician visits (Visits) in the past year, controlling for selected demographics and comorbidities.

Of the 15,258 participants, 1,562 (21%) had CKD stages I-IV (2,110 [13.8%] stages I-II [early] and 1,121 [7.3%] stages III-IV [late]). Mean (SE) Hosp was 0.17 (0.008) and Visits was 3.74 (0.08). Increasing age, decreasing hemoglobin (Hb) level, and an increasing prevalence of comorbidities were associated with increasing CKD stage. With increasing CKD stage, there were increases in both Hosp (mean [SE]: no CKD, 0.15 [0.01]; early CKD, 0.19 [0.01]; late CKD, 0.42 [0.03]) and visits (no CKD, 3.51 [0.08]; early CKD, 4.43 [0.18]; late CKD, 6.53 [0.38]), a trend which was consistent across patient characteristics. Results from multivariate analyses suggest that even after controlling for comorbid diseases, insurance coverage, and patient characteristics, patients with later stages of CKD were more likely to have a Hosp (OR=2.12, 95% CI: 1.66, 2.71) or more than 3 Visits (OR=1.81, 95% CI: 1.46, 2.23) compared with those with no CKD; those with higher Hb were less likely to report a Hosp (OR=0.88, 95% CI: 0.82, 0.95) or have more than 3 Visits (OR=0.89, 95% CI: 0.85, 0.94) compared with those with lower Hb.

In this population-based sample, anemia and worsening CKD were independently associated with increased health care utilization, suggesting that health care utilization could be reduced with early recognition and treatment of both CKD and anemia.

PREDICTORS OF CONSISTENT IN-TARGET HEMOGLOBIN OVER THE TRANSITION TO DIALYSIS

Tom Arneson[1], Melissa Skeans[1], Stephan Dunning[1], Michael del Aguila[2], David Gilbertson[1], Allan Collins[1]. [1]Chronic Disease Research Group, Minneapolis Medical Research Foundation, Minneapolis, Minnesota, USA, [2]Roche Laboratories Inc., Nutley, New Jersey, USA.

As chronic kidney disease patients transition into dialysis, anemia control can be difficult. Factors associated with maintaining consistent hemoglobin (Hb) levels over the transition period are unknown.

We identified 7069 dialysis patients, aged 67 years or older, incident from January 1, 1998, to September 30, 2003. Target Hb levels were defined for each of 3 periods: (1) 10 to 12 g/dL for the 3 months before initiating dialysis and (2) the month of initiation, and (3) 11 to 12.5 g/dL in month 3 after initiation. Patients were classified as above (A), in (T), or below (B) target Hb for each period. We used logistic regression to identify predictors of consistent in-target Hb over all periods (TTT).

TTT (22%) was the most common group; 57% of patients were in-target at least 2 periods; 6.8% were BBB. Probability of consistent in-target Hb was increased for patients with 8-12 months on ESAs (OR= 1.20), while African Americans were 25% less likely to remain in-target (OR= 0.75).

Predictor of Consistent In-Target Hb	OR (95%CI)	*P*-value
Cystic kidney disease as 1˚ diagnosis	1.62 (1.13,2.34)	0.0094
Albumin > 3.4 g/dL at initiation	1.21 (1.08,1.37)	0.0015
8 to 12 months on ESA (vs. 1 to 7)	1.20 (1.03,1.40)	0.0059
< 1 month on ESA (vs. 1 to 7)	0.89 (0.74,1.07)	0.0132
Avg. weekly ESA > 10,000 units*	0.83 (0.72,0.95)	0.0087
ESRD initiation year < 2000	0.82 (0.72,0.93)	0.0014
Comorbid GI disease*	0.82 (0.67,1.00)	0.0464
Comorbid COPD*	0.81 (0.69,0.96)	0.0160
African American (vs. other race)	0.75 (0.64,0.88)	0.0003
eGFR < 5 mL/min/1.86 m^2 at initiation	0.68 (0.55,0.85)	0.0005

* 3 months prior to initiation of dialysis

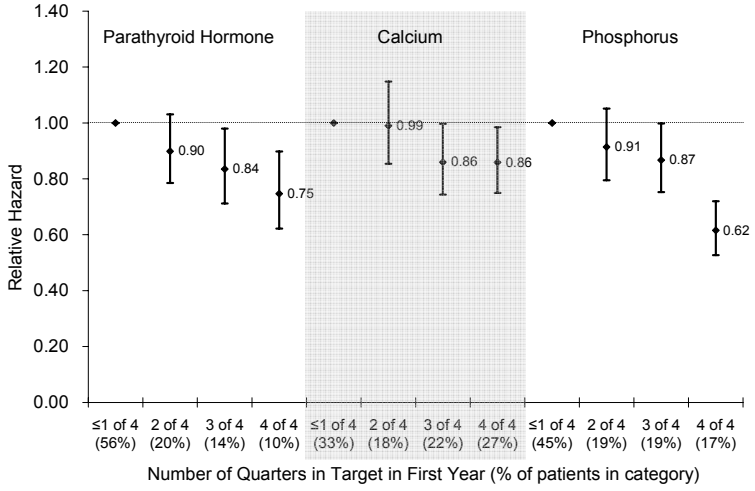
One in 5 patients remained in-target throughout transition, and 57% remained in-target 2 periods or more. Those with less disease burden were better able to maintain consistent in-target Hb levels.

SUSTAINED CONTROL OF PARATHYROID HORMONE (PTH), CALCIUM (CA), AND PHOSPHORUS (P) MAY IMPROVE SURVIVAL IN HEMODIALYSIS (HD) PATIENTS

Vasily Belozeroff[1], Mark Danese[2], Karen Smirnakis[1], Kenneth J Rothman[3]; [1]Amgen Inc, Thousand Oaks, CA; [2]Outcomes Insights Inc, Newbury Park, CA; [3]RTI Health Solutions, Research Tri Park, NC

We studied the association between consistency of PTH, Ca, and P control and risk of death in patients (pts) who started HD at a large US provider in 2000-2002. We assessed the number of calendar quarters (qtrs) over the first year of HD in which KDOQI targets were achieved for PTH (150-300 pg/mL), Ca (8.4-9.5), and P (3.5-5.5) mg/dL. In 17,828 pts followed for up to 3 years, we assessed survival time by number of qtrs in control using proportional hazards model adjusted for age, sex, race, body mass index, hemoglobin, blood pressure, albumin, urea reduction ratio, and diabetes. Achievement of a target for all 4 qtrs was associated with the lowest risk of death. We observed an inverse relation between the number of qtrs in target and the risk of death (Figure). Our results suggest that consistent control of PTH, Ca, and P in KDOQI targets may help reduce mortality in HD pts.

Relative risk of death by number of quarters in KDOQI targets



TRENDS IN PARATHYROID HORMONE (PTH) IN HEMODIAYSIS (HD) PATIENTS (PTS)

Vasily Belozeroff[1], Rohit Borker[1], Beth Barber[1], Lara Pupim[1], Raymond Hakim[2]; [1]Amgen Inc, Thousand Oaks, CA; [2]FMC NA, Lexington, MA

Secondary hyperparathyroidism (HPT) is a prevalent complication of chronic kidney disease, yet little data are available on progression of secondary HPT in clinical practice. The goal of our study was to assess the distribution and trends of PTH levels in HD pts. We analyzed data from a random sample of HD pts treated at a large provider in the US between 2000 and 2004 using only one type of PTH assay. In pts who survived ≥1 year in the study, we assessed mean PTH over a 3-month period at enrollment and after 6 months, and calculated the percentage of pts within each of 5 PTH categories related to disease severity (PTH <150, 150-300, 301-500, 501-800, >800 pg/ml), and the percentage of pts who moved between categories. Among 35,825 HD pts, 26% to 61% remained within the same category after 6 months, particularly in the highest and lowest categories; 41% of pts with PTH >300 at enrolment moved down at least one category, and 36% of pts with PTH in 150-800 moved up at least one category. (Table) Our results suggest substantial intra-subject PTH movement in HD pts, which may be due to the differences in pt characteristics and therapeutic regimens. Studies are needed to characterize secondary HPT progression and identify therapeutic approaches for the optimal control of PTH levels.

Percentage of pts moving between PTH (pg/ml) categories

PTH	After 6 months					
At enrollment	< 150	150 to 300	301 to 500	501 to 800	> 800	Total
< 150	47.6	34.4	13.0	4.1	0.9	41.0
150 to 300	21.4	39.3	25.2	11.0	3.1	29.9
301 to 500	12.3	28.0	27.1	21.9	10.7	15.5
501 to 800	7.2	15.3	21.0	26.1	30.4	8.3
> 800	6.4	7.2	9.4	15.3	61.7	5.2
Total	28.8	31.9	19.3	11.3	8.7	100

TRENDS IN THE PROPORTION OF TRANSPLANTATION AMONG PREVALENT CASES OF DIABETES-RELATED END-STAGE RENAL DISEASE, BY RACE, UNITED STATES, 1995–2004. Nilka Ríos Burrows, Yanfeng Li, Linda Geiss, Desmond Williams, Centers for Disease Control and Prevention, Atlanta, GA, USA.

In 2004, more than 170,000 people with end-stage renal disease due to diabetes (ESRD-DM) in the United States were living on chronic dialysis or with a kidney transplant. National health objectives aim to increase the proportion of patients on dialysis who register for kidney transplantation. We examined racial-specific trends in the proportion of prevalent ESRD-DM cases having had transplantation.

We used data from the United States Renal Data System to obtain the number of prevalent ESRD-DM cases between 1995 and 2004 by treatment modality and race. Joinpoint regression analysis was used to assess trends.

From 1995 to 2004, the trend in the proportion of prevalent ESRD-DM cases with a transplant varied by race. Among non-whites, it increased significantly among Native Americans (10.8% to 13.3%), Asian Americans (8.4% to 11.8%), and blacks (7.5% to 9.7%). Increases for Asian Americans and blacks were steeper in recent years. On the other hand, among whites, the proportion with transplantation decreased from 1995–1997 (24.3% to 23.3%), leveled off from1997–2000, and slowly increased from 2000–2004 (22.7% to 23.2%).

The dissimilar trends between whites and non-whites resulted in a narrowing of racial disparities in the proportion of cases having had a transplant. However, non-whites continue to have a lower proportion of transplantation compared with whites. Because persons who successfully receive a transplant have improved quality of life and survival, continued efforts are needed to increase transplantation among all racial groups, particularly non-whites.

THE RIGHT START KNOWLEDGE TEST: A KIDNEY KNOWLEDGE SURVEY FOR HEMODIALYSIS PATIENTS.

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Greater knowledge predicts adherence to diet, better self-reported mental health, and lower serum phosphorus in chronic hemodialysis (CHD) patients. Measurement of knowledge is difficult. There are few tests of general kidney knowledge and only one was designed for CHD patients. This study aims to describe the development, reliability, and clinical associations of the Right Start Knowledge Test (RSKT).

The RSKT is a 23-item, multiple-choice response survey, that evaluates awareness of recommendations and complications of CHD. It was developed from contributions of experts and patients. The test was given to 878 incident CHD patients, from 39 dialysis clinics from 2002-2004. Clinical variables were collected at baseline.

Good internal reliability of the RSKT was shown (Cronbach's alpha = 0.74). Factor analysis found one predominant factor with an Eigen value of 4.3. Overall mean (SD) percent correct score was 64%(19%). In unadjusted analysis, lower scores were associated with older age (Q1: 67% vs. Q4: 57%; p=0.0002) and non-white (NW) race (W:64% vs. NW:60%; p=0.02). No differences were found by gender or diabetes status. Low knowledge scores were associated with the use of catheters as baseline access type (Catheter: 62% vs. AVFistula: 67%; p=0.05). No associations were found with baseline hematocrit, iron studies, serum albumin, phosphorus, or intact-parathyroid hormone measures.

In summary, the RSKT is a reliable measure of general kidney knowledge and overall scores of knowledge are moderate. CHD patients at risk for low kidney knowledge may be older and non-white race, and low knowledge may be associated with poor self-care behavior in the area of vascular access.

TRADITIONAL ESRD BIOMARKERS MAY HAVE LOWER PREDICTIVE VALUE FOR MORTALITY THAN NON-TRADITIONAL BIOMARKERS: A SYSTEMATIC REVIEW OF THE LITERATURE

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Purpose: Despite data that traditional dialysis biomarkers are improving over time (*e.g.* Hct, albumin, PTH), USRDS data indicate that mortality rates are not improving in lockstep with these quality enhancements. With increased focus on clinical performance measures based on traditional biomarkers, there has been less emphasis on other biomarkers that may also strongly predict mortality. We sought to perform a systematic review to identify and quantitatively rank-order the predictive value of all published biochemical markers in dialysis.

Methods: We conducted a structured search of MEDLINE to identify studies that provide data about the dichotomous effect size of a biochemical predictor of mortality in dialysis. Independent reviewers performed title and abstract selections using *a priori* criteria, and subsequently abstracted data from each selected manuscript. We then calculated the sample size-weighted pooled effect size (RR or HR) of death with dichotomized "high" *vs.* "low" levels of each biomarker, using the weighted mean effect size as our point estimate.

Results: There were 5171 titles, of which 128 (representing 44 biomarkers) were selected. Natriuretic peptides (ANP, BNP) had the largest effect size, as the pooled HR of death for patients with high *vs.* low levels was 9.45. In order of decreasing pooled effect size: serum creatinine (RR=3.85), troponin T (RR=3.69), CRP (RR=3.23), homocysteine (RR=2.78), pre-albumin (RR=2.44), and IL-6 levels (RR=1.83). The pooled RR for traditional biomarkers was lower: albumin (RR=1.8), Hct (1.37), Ca*PO4 (RR=1.27), and PTH (1.19).

Conclusions: Quality improvement efforts to improve traditional biomarkers in ESRD are necessary, but likely insufficient, to improve overall mortality in dialysis. Renewed consideration of cardiovascular, inflammatory, and nutritional biomarkers that are especially strong predictors of mortality may have important implications for risk stratification and targeted therapeutic interventions in the dialysis population.

ECONOMIC IMPACT OF CARDIOVASCULAR DISEASE AND FRACTURES IN PATIENTS WITH ESRD. Quan V Doan[1], Michelle Dylan[1], Robert Griffiths[1], Rohit Borker R[2], Beth Barber[2], John Kim[2], Robert W Dubois[1] ; 1:Cerner LifeSciences, Beverly Hills, CA, USA, 2: Amgen Inc., Thousand Oaks, CA, USA. The costs of cardiovascular disease (CVD) and fractures are well documented, however, the cost of these events in patients with end-stage renal disease (ESRD) are not. This research quantified the cost of CVD, limb amputation and fractures among ESRD patients using Medicare claims data from 2001 from the United States Renal Data System. Diagnosis, procedure and DRG codes were used to identify the events and conditions. The acute events include costs for hospitalization, SNF, physician services, and institutional outpatient services. Annualized costs were reported for chronic conditions as cost per person year. Costs were reported in 2004 US dollars. Only costs related to the events or conditions of interest were included. Drug- and dialysis-related costs were not included. The five most costly acute events (cost/episode) and five most costly chronic events (cost/person-year) are reported (table). The economic burden of CVD and fractures in ESRD patients was substantial. These data will be used to build an economic model.

Acute Event	N	Cost/episode	(SD)
Heart valve repair	109	$89,318	($86,731)
Heart valve replacement	943	$70,900	($60,153)
Peripheral Vascular Disease	39,007	$25,667	($25,634)
Limb amputation	7550	$24,398	($24,427)
Hip fracture	2600	$20,810	($16,743)
Chronic Condition	**Patient Year**	**Cost/person year**	**(SD)**
Heart Valve Disease	3,413	$36,333	($78,698)
Peripheral Vascular Disease	21,952	$33,628	($60,587)
Coronary Heart Disease	24,204	$30,890	($85,047)
Arrhythmia	19,357	$30,664	($215,819)
Stroke	9,226	$25,035	($80,419)

CORRELATES OF CHRONIC KIDNEY DISEASE (CKD) AMONG HISPANIC SUBGROUPS: RESULTS FROM THE KIDNEY EARLY EVALUATION PROGRAM (KEEP)

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Mexican Americans (MAs), Puerto Ricans (PRs), and Cuban Americans (CAs) are often combined as "Hispanics" in data analyses. We evaluated correlates of CKD, and control of risk factors for CKD progression and/or cardiovascular disease, for these subgroups.

We examined the prevalence of anemia and microalbuminuria, alongwith hypertension (HTN) control and diabetes (DM) control among MAs (n=1027), PRs (n=439) and CAs (n=55) with CKD in the KEEP study. KEEP is a CKD screening program enrolling individuals $\geq$18 years with DM or HTN, or a family history of CKD, DM or HTN. CKD was evaluated by estimated glomerular filtration rate and urinary dipstick estimation of albuminuria. We used logistic regression models to estimate the odds of HTN and DM control along with 95% confidence intervals, for MAs and PRs compared to non-Hispanic whites (The CA subgroup was too small to retain in the multivariate model). We adjusted these analyses for age, gender, and CKD stage.

We found no difference in the prevalence of anemia by subgroup (MAs 6.2%, PRs 6.2%, CAs 5.5%, p=0.97), but did observe a difference in microalbuminuria (MAs 89.9%, PRs 85.0%, CAs 78.2%, p=0.002). Among participants with self-reported HTN, we found no difference in the odds of elevated blood pressure for MAs (0.94, 0.76-1.14) or PRs (1.07, 0.80-1.44) compared to non-Hispanic whites. Among participants with self-reported DM, PRs (1.60, 1.19-2.16) had greater odds of elevated blood glucose than non-Hispanic whites, while no difference was seen for MAs (1.10, 0.90-1.34).

Our findings suggest that important distinctions in the clinical picture of CKD among Hispanics may be obscured without examining data by specific subgroups.

UNDERESTIMATION OF CHRONIC KIDNEY DISEASE (CKD) BY MEASURED SERUM CREATININE: DATA FROM THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (NHANES 1999-2002)

O. Kenrik Duru[1], Dulcie Kermah[2], Allen Nissenson[1], and Keith Norris[1,2]. [1]Geffen School of Medicine at UCLA, Los Angeles, CA; [2]Charles R. Drew University of Medicine/Science, Los Angeles, CA.

Serum creatinine concentrations may overestimate renal function among selected populations, and delay appropriate management of CKD. We provide national estimates of proportions of Stage III CKD despite normal creatinine values.

Study subjects were NHANES participants with serum creatinine from 0.7 to 1.5 mg/dl, the accepted normal range at most laboratories, as our analytic sample (n=7547). Estimated glomerular filtration rate (eGFR), derived from the Modification of Diet in Renal Disease formula, was used as a measure of renal function, and the Kidney Disease Outcomes Quality Initiative staging criteria were used for CKD stage assignment. Using logistic regression analysis, we determined the odds of Stage III CKD compared with Stage I CKD or no CKD, despite normal creatinine and after adjusting for race, gender, and age.

Among those under 65 years of age, 4% overall, 6% of whites, and 7.5% of women, had normal creatinine but Stage III CKD. Among those 65 years and over, 26% overall, 29% of whites, and 36% of women, had normal creatinine but Stage III CKD. The sensitivity of creatinine was especially poor in the setting of chronic disease among those 65 years and over, as 30% with hypertension, 33% with diabetes, 36% who have had a myocardial infarction, and 45% with congestive heart failure had Stage III CKD despite normal creatinine values.

In multivariate analyses, hypertension (Adjusted Odds Ratio/AOR 2.2, 95% CI 1.7-2.9), diabetes (AOR 2.3, 1.4-3.9), history of a myocardial infarction (AOR 2.9, 1.8-4.8), and congestive heart failure (AOR 3.4, 1.9-6.1), were associated with elevated odds of Stage III CKD despite a normal serum creatinine measurement.

Serum creatinine alone has poor sensitivity for relatively advanced CKD among the elderly, especially for whites, women, and those with chronic conditions. Estimated GFR is a superior means of evaluating renal function.

THE ASSOCIATION OF IRON ADMINISTRATION WITH HEMOGLOBIN OVERSHOOTING, David T. Gilbertson, Rui Zhang, Stephan Dunning, James Ebben, Tom Arneson, Allan J Collins. Chronic Disease Research Group, Minneapolis, MN, USA.

Dialysis facility protocols for iron management are generally separate from protocols for anemia management, which may contribute to hemoglobin (Hb) variability and hemoglobin overshooting. The purpose of this study was to investigate the effect of iron administration on hemoglobin overshooting.

The cohort studied included 149,292 hemodialysis patients (pts) point prevalent on Jan.1, 2004, surviving through Jun 30, 2004, with Medicare as primary payer, and with valid EPO claims in Apr-Jun. Jan-Apr were used to characterize comorbidity, and pts were defined as receiving maintenance iron if they received iron in each month Jan-Mar. Logistic regression was used to assess the effect of iron administration in month 4 with overshooting Hb of 12, 13 or 14 g/dL in months 5 or 6, adjusting for pt characteristics, comorbidities, Hb level in month 4, and EPO dose in month 4.

Factors associated with overshooting Hb levels of 12, 13, or 14 g/dL included higher Hb in month 4, higher EPO dose, iron administration in month 4, iron administration in months 1-3, and older age. Although any iron administration increased the probability of overshooting, the relationship was strongest among pts who were not receiving maintenance iron. Iron is an independent predictor of Hb overshooting in CKD patients on dialysis. Given recent clinical trials results suggesting possible adverse outcomes among patients when targeting Hb levels above 13, this analysis suggests that clinicians should give more consideration to the potential impact of intermittent iron dosing as it relates to Hb overshooting and variability.

Hemoglobin Overshooting in Months 5 or 6

		Hb ≥ 12 g/dl	Hb ≥ 13 g/dl
		Odds Ratio (95% CI)	**Odds Ratio (95% CI)**
Iron			
No iron in month 4	No iron mos. 1-3	1.00	1.00
	Iron mos. 1-3	1.10 (1.04,1.16)	1.16 (1.09,1.23)
Iron in month 4	Iron mos. 1-3	1.27 (1.23,1.30)	1.26 (1.22,1.29)
	No iron mos. 1-3	1.49 (1.45,1.54)	1.43 (1.39,1.48)

MODERATE CHRONIC KIDNEY DISEASE AND COGNITIVE FUNCTION IN ADULTS 20-59 YEARS OF AGE (NHANES III)

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Previous studies among elderly suggest an association between chronic kidney disease (CKD) and cognitive impairment. The purpose of this study was to determine whether moderate CKD is associated with cognitive performance among young, healthy, ethnically diverse adults.

Three computerized cognitive function tests of visual-motor reaction time (Simple Reaction Time), visual attention (Symbol Digit Substitution), and learning/concentration (Serial Digit Learning) were administered to a random sample of participants, aged 20-59 years, who completed initial interviews and medical examination in the National Health and Nutrition Examination Survey III. Participants for this study (n=4,849) completed at least one cognitive function test. Glomerular filtration rate (GFR) was estimated using the Modification of Diet in Renal Disease equation. Moderate CKD was defined as estimated GFR (eGFR) 30-59 mL/min/1.73m^2. Unadjusted, residual-adjusted, and multivariate-adjusted logistic regression models were used.

The cohort was 49.0% male, 11.6% Black, and mean ± SE age was 37.2 ± 0.23 years and eGFR 105.5 ± 0.73 mL/min/1.73m^2. There were 31 prevalent cases of moderate CKD (0.8%). Models were adjusted for residual effects of age, sex, race, diabetes, and other known potential confounders. In multivariate models, moderate CKD was not significantly associated with reaction time, but was significantly associated with learning/concentration (OR: 2.41; 95% CI: 1.30, 5.63) and impairment in visual attention (OR: 2.74; 95% CI: 1.01, 7.40).

In summary, among those in a large nationally representative sample of healthy, ethnically diverse 20-59 year-old adults, moderate CKD, reflected by eGFR 30-59 ml/min/1.73m^2, was significantly associated with poorer performance in visual attention and learning/concentration.

USE OF A CLINICAL ALERT AND REMINDER SYSTEM TO PROMOTE K/DOQI BONE GUIDELINE IMPLEMENTATION

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The National Kidney Foundation developed the Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guidelines to help guide the management of patients with chronic kidney disease (CKD). However, surveys of current clinical practice continue to identify quality-of-care deficits. For example, estimates of PTH testing in patients with CKD stages 3 and 4 range from 1% to 30%.

We developed a claims-triggered clinical alert and reminder system to communicate potential clinical opportunities to the primary care provider. These messages were derived from the recent KDOQI guidelines (e.g. calcium, phosphorus and PTH monitoring in CKD patients). Following communication of the alert, compliance with the guideline recommendation was measured using claims-based data during a pre-established evidence time window.

Patients with CKD stages 3 and 4 received 470 and 193 alerts per 100,000 patient-years of enrollment, respectively, during the observation period from November 2005 through June 2006. Delivery of the alert was followed by objective evidence of implementation of calcium, phosphorus or PTH monitoring in 40% of CKD stage 3 patients and 47% stage 4 patients.

A technology-driven claims-based clinical alert system can be used to identify gaps in care and leads to improved guideline implementation.

COST-EFFECTIVENESS OF EPOETIN ALFA IN PATIENTS ON CHRONIC KIDNEY DIALYSIS

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There is debate concerning optimum dosing of recombinant human erythropoietin (EPO) to raise hemoglobin (Hb) and alleviate symptoms of anemia. We compare the relative cost-effectiveness of alternative dosing regimens to achieve target Hb levels of 11.0 – 12.0 g/dL and 12.0 – 13.0 g/dL relative to a target of 9.5 – 10.5 g/dL. The upper end of this range is below the target Hb level associated with adverse patient outcomes in recently reported trials of anemia management in a pre-ESRD cohort.

Analysis is based on a Markov model that simulates the course of treatment for ESRD patients who initiate hemodialysis with a baseline Hb in the 9.5 – 10.5 g/dL range. Patients are assumed to receive EPO via intravenous route during 3 – 4 times weekly dialysis sessions over 20-year maximum follow-up. Model parameters integrate available clinical trial evidence with extensive data from observational studies.

Incremental cost per quality-adjusted life year (QALY) for the 11.0 – 12.0 g/dL strategy relative to 9.5 – 10.5 was $46,259. The incremental cost to raise Hb to the 12.0 – 13.0 g/dL range relative to 11.0 – 12.0 was $42,276. Considerable uncertainty surrounds these estimates due to the lack of prospective studies that conclusively establish the effects of Hb levels on outcomes such as mortality, morbidity, and quality of life.

Model results suggest that an Hb target range of 12.0 – 13.0 g/dL improves patient outcomes at an acceptable cost to society.

ADHERENCE TO K/DOQI GUIDELINES FOR BONE METABOLISM & DISEASE IN CHRONIC KIDNEY DISEASE. Tracey Hoy[1], Maxine Fisher[1], Rohit Borker[2], Beth Barber[2], Brad Stolshek[2], William Goodman[2] (1) HealthCore, Inc. Wilmington, DE, USA; (2) Amgen, Inc. Thousand Oaks, CA, USA. Recent research has shown chronic kidney disease (CKD) is associated with poorer health outcomes and high medical expenditures and that early detection and treatment may prevent or delay adverse outcomes. The Kidney Disease Outcomes Quality Initiative (K/DOQI™) guidelines for bone metabolism and disease were developed to improve the management of patients (pts) with CKD. This research investigated adherence to K/DOQI™ guidelines for frequency of testing and for the control of parathyroid hormone (PTH), calcium (Ca) and phosphorus (P). The analysis was performed with pooled data from two large US managed care databases. Pts were identified from June 1, 2002 to May 31, 2004 based on laboratory data. Pts were excluded if they were < 18 years or ≥ 65 years of age, had less than 18 months of continuous eligibility, or had renal cancer. A total of 9,196 pts with CKD stages 3 or 4 (8,875 and 321, respectively) were identified. Ca levels were tested in accordance with K/DOQI™ guidelines in 95.6% of pts with stage 3 CKD. The percentage dropped among pts with stage 4 CKD (43.3%), when K/DOQI™ guidelines recommend increasing the frequency of testing from 1x/year to 4x/year. Frequency of testing PTH and P was low (Table). Among those tested a high percentage of pts were within K/DOQI™ ranges for Ca and P for both stages 3 and 4. However, < 40% of those with measured PTH levels were within the K/DOQI™ target ranges.

	PTH		Ca		P	
	CKD3	CKD4	CKD3	CKD4	CKD3	CKD4
Pts tested as per K/DOQI™ %	1.8	0.3	95.6	43.3	4.8	1.6
Pts with ≥ 1 lab per year %	1.8	7.2	95.6	97.5	4.8	20.3
Pts with ≥ 1 lab in target range %	38.5	26.1	99.1	96.8	91.5	89.2

These data demonstrate that there remains substantial opportunity to improve the quality of care with regard to mineral metabolism for pts with CKD.

ACUTE RENAL FAILURE AND PREDICTORS OF MORTALITY IN PATIENTS WITH CONGESTIVE HEART FAILURE RECEIVING NESIRITIDE.

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A recent meta-analysis has suggested that Nesiritide (NES) is associated with an increased risk of death, possibly related to the development of acute renal failure (ARF).

We examined the relationship between NES and 60-day mortality among 1410 consecutive CHF patients. We then used univariate and multivariate analysis to determine risk factors for 60-day mortality in a cohort of 685 of the original 1410 patients, for whom we had sufficient clinical and laboratory data.

Univariate analysis of both the 1410 consecutive CHF patients and the 685 patient cohort confirmed that NES was associated with an increase in mortality: n=1410, 10% vs. 6%, p=0.013, odds ratio (OR) 1.045, 95% C.I. 1.005-1.086; n=685, 19% vs. 12%, p=0.043, OR=1.60, 95% CI 1.012-2.54. Of the 685 patients, 175 (25%) received NES. We stratified ARF into two categories based on the rise in serum creatinine (SCr): >0.3 mg/dL or >0.5 mg/dL. As in our recent publication, but in contrast to a recent meta-analysis, there was no difference in the incidence of ARF between patients receiving vs. not receiving NES by either definition (34% vs. 31%, p=0.388; 16% vs. 14%, p=0.54). Forward stepwise regression analysis failed to reveal NES usage as an independent predictor of mortality, but did reveal the following independent predictors: ARF, absence of beta-adrenergic blockade, admission BUN, digoxin use, and admission BNP. Since NES alone independently predicted neither ARF nor mortality, we looked for an interaction among these variables. Strikingly, in CHF patients with ARF (rise in SCr >0.5 mg/dL), forward stepwise regression analysis revealed that NES was the sole significant predictor of mortality (p=0.006, OR=3.73, 95% CI 1.45-9.56).

We conclude that, while NES *per se* is not associated with an increased risk for death or ARF, the development of ARF in conjunction with NES may confer an increased risk of mortality.

RISK FACTORS FOR PROGRESSION OF KIDNEY DISEASE: A LONGITUDINAL STUDY IN A COMMUNITY PRACTICE

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The purpose of this study was to examine the effect of blood pressure on the decline of kidney function using electronic medical records. Patients 18 years or older were included if they had at least 2 serum creatinines measured at one year interval. MDRD glomerular filtration rates (GFR) at baseline (BL) and follow-up (FU) were calculated as well as the slope of the GFR changes and the systolic and diastolic follow-up BP averages. BL-BP was stratified into 4 stages; Normal: BP<140/90; Mild: 140-159/90-99; Moderate:160-179/100-109 Severe: ≥180/110. A logistic regression was used to estimate the association between the decline in GFR defined as a slope<0 (dependent variable) and BP stages after adjusting for BL GFR, age, race, sex, diabetes.

A total of 4,253 patients were eligible. The median FU time was 3.3 years (max 7.8 years). Below are the population characteristics.

	Normal (55.6%)	Mild (32.1%)	Moderate (10.3%)	Severe (2.1%)
Female (%)	63.6	63.4	66.8	70.8
Black (%)	38.1	47.5	48.3	50.6
Age (Mean years)	53.4	57.0	58.7	62.4
Diabetes (%)	22.5	23.0	22.4	30.3
FU SBP (Mean)	**125**	**135**	**140**	**145**
FU DBP (Mean)	**76**	**81**	**83**	**83**
Decline in GFR (%)	39.7	44.8	47.6	58.4

The adjusted odds ratios (OR) and 95%CI associated with BP stages were 1.2 (1.1-1.4), 1.4 (1.1-1.7), and 2.0(1.3-3.2) for mild, moderate, severe compared to normal BP. Other risk factors included age, being black (OR=1.2 (1.1-1.4)) and having diabetes (OR=1.8 (1.5-2.1)).

Although the average follow-up SBP and DBP were within or slightly higher normal ranges, patients with high baseline BP were more likely to experience a GFR decline than those with normal baseline BP suggesting that more aggressive BP treatment is warranted especially in patients with severe baseline BP.

INVESTIGATION OF NEPHROGENIC FIBROSING DERMOPATHY AND ASSOCIATION WITH GADOLINIUM-CONTAINING MRI CONTRAST

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Nephrogenic Fibrosing Dermopathy (NFD) is a fibrosing disorder of unknown etiology that has been described in patients with renal disease. In May 2006, a cluster of NFD was identified at a hospital in Missouri. An investigation and case control study were conducted to identify risk factors for NFD.

Case-patients were identified from hospital records. A confirmed case-patient was defined as a patient identified between January 2002 and August 2006 with clinical and pathologic findings of NFD. Confirmed case-patients and controls that had sufficient information covering the 6 months prior to diagnosis were included in the case-control study. Three controls were matched to each case by location and date of NFD diagnosis.

A total of 28 cases were identified. Confirmed case-patients (n=19) and controls (n=57) were included in the case-control study. Case-patients and controls were similar with respect to demographic characteristics. In univariate analysis, exposure to gadolinium-containing MRI contrast in the preceding year (MOR 7.99, 95% CI 2.22-28.77); presence of dependent edema (MOR 7.11, 95% CI 1.95-25.82); history of deep venous thrombosis (MOR 5.05, 95% CI 1.25-20.42); and hypothyroidism (MOR 4.10, 95% CI 1.14-14.70) were all associated with NFD. Case-patients were not more likely than controls to be on high-dose epoetin alfa. In multivariate analysis, exposure to gadolinium-containing MRI contrast in the prior year (MOR 8.97, 95% CI 1.28-63.01) remained associated with NFD.

In this study, exposure to gadolinium-containing contrast was highly associated with NFD. Use of these agents should be avoided except when medically necessary in patients with advanced renal disease.

BONE MINERAL DENSITY (BMD) AND CHRONIC KIDNEY DISEASE (CKD): IS THERE A RELATIONSHIP, A RETROSPECTIVE ANALYSIS

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Introduction: The association of kidney function with BMD has remained conflicting and confusing. A Retrospective analysis of DEXA data, eGFR, iPTH and 25 OH Vitamin D assessed this relationship.
Methods: Patients were partitioned into two categories (eGFR ≤ 60, those with CKD and eGFR > 60, those without CKD).
Results: The distribution of males and females in the two groups were equivalent (p = 0.914). However, there was a significant difference in ages (67.8 ± 1.4 vs 60.2 ± 0.7, p = 0.001). This difference prompted an analysis of covariance to adjust for the differences in age. The T-score difference between the CKD and non-CKD groups were highly significant for the wrist (p = 0.001). The age-adjusted means ± standard deviations (sample size) are reported below.

		eGFR > 60	eGFR ≤ 60	p-value
Sex	Male (n, %)	53 (79.1%)	14 (20.9%)	
	Female (n, %)	388 (79.7%)	99 (20.3%)	0.914
Age		67.8 ± 1.4 (441)	60.2 ± 0.7 (113)	0.001
DEXA T-score				
Wrist		-0.95 ± 0.08 (239)	-1.37 ± 0.15 (67)	0.011
iPTH		60.9 ± 12.9 (38)	148.1 ± 17.8 (20)	0.001
Calcium		9.3 ± 0.5 (436)	9.4 ± 0.6 (110)	0.047
25 OH Vit D		20.0 ± 1.5 (51)	26.3 ± 2.4 (20)	0.346

A significant doubling of the intact PTH was documented in the CKD group despite the presence of global 25 OH Vitamin D deficiencies (defined as a level < 30) in both groups. No significant difference in Vitamin D data was found between the 2 groups (p = 0.346).
Conclusion: The relationship of this very impressive greater the doubling of the iPTH in the CKD group coupled with a significant decrease in BMD will require further prospective studies. Also, the therapeutic efficacy of normalization of the iPTH on improving bone mineralization would also warrant further study from this data. Therapy to normalize the 25 OH Vitamin D appears to be needed in both groups. This data also suggests the need to assess for the presence of CKD in all patients with bone demineralization along with the iPTH and vitamin D status.

ASSOCIATION OF CHRONIC KIDNEY DISEASE WITH BIRTH WEIGHT AND GENDER IN THE KIDNEY EARLY EVALUATION PROGRAM PARTICIPANTS

Suying Li[1], Shu-Cheng Chen[1], George Bakris[2], Peter A. McCullough[2], Claudine Jurkovitz[2], Andrew Narva[2], Janet McGill[2], Michael Klag[2], Wendy Brown[2], Keith Norris[2] and Allan Collins[1]. [1]Chronic Disease Research Group, Minneapolis, MN. [2]KEEP Steering Committee, National Kidney Foundation, New York, New York, United States.

This study examines the association of chronic kidney disease (CKD) and birth weight (BW) in the Kidney Early Evaluation Program (KEEP) Participants. About 32% KEEP participants wrote down BW in their questionnaires. We included persons with BW>1 pound (lb) and age between 18 to 75 years. We analyzed association of CKD with BW stratified by gender. The BW (lbs) was categorized into >1-5, >5-6, >6-7 (median), >7-8, >8-9, and >9.

Among 10,784 eligible participants, the prevalence of CKD was 24.6%. Low BW was consistently associated with higher risk of CKD across age, gender, race, and chronic conditions. Multivariate analyses showed that gender and BW interactively associated with CKD. The following table shows the CKD rates and odds ratios by interaction of gender and BW.

		Unadjusted CKD rate (%)		Adjusted odds ratio^	
BW (lb)	N	Male (N=2538)	Female (N=8246)	Male (N=2538)	Female (N=8246)
>1 to 5	1464	31.0	26.6	1.82*	1.54*
>5 to 6	1955	26.0	25.1	1.61*	1.52*
>6 to 7	3010	18.8	25.0	1.00 (ref)	1.50*
>7 to 8	2449	21.4	23.3	1.10	1.37*
>8 to 9	1116	21.3	27.3	1.07	1.64*
>9	790	26.8	25.2	1.42*	1.33

*significant at 5% level; ^ adjusted for age, race, insurance, education, region, chronic conditions, and family history of KD; p-value for interaction of gender and BW is 0.0079

In male KEEP participants, BW lower than 6 lbs or greater than 9 lbs was significantly associated with higher risk of CKD; in females, BW was not significantly associated with CKD.

EARLY INTERVENTION PROGRAM: AN EVALUATION

mallery, carmen, overland park, ks; cahill, molly, overland park, ks; awad, ahmed, overland park, ks; whitlock, robert, columbia, mo.

The National Kidney Foundation of Kansas and Western Missouri has conducted an early intervention project (EIP) in Kansas & Western Missouri. Minority populations were targeted. In 1998 the EI Committee developed a screening protocol to identify persons with high blood pressure, diabetes, obesity and /or microalbuminuria. When one or more health risks were identified, participants were counseled and referred to a primary care provider for follow-up. The goal of the program is to intervene early in the disease process that results in later development of CKD. Besides the cost effectiveness of an approach, the savings in pain and suffering for patients are incalculable by avoiding expensive and difficult treatment of ESRD. The purpose of this evaluation is to discuss findings between the summer of 1998 to the fall of 2005. The data, including, blood pressure, blood glucose and microalbumin and comparison with ethnicity, new findings of risk factors, comorbididies disclosed during screening, level of education, gender and age. Furthermore, to include follow-up of these variables on individuals that were referred to a primary care provider.

Of the screened patients (n=7488). Of the 7488, **49% (3660)** ***had one or more*** risk factors and **27% (2010)** ***did not know*** they had risk factors. Curiosity for the program was the most common reason the participant attended the screening (38%) while having high blood pressure was the second motive to attend (28%) and diabetes (18%). Given the size of the sample (n=7488), this reinforces general impressions that many people are going about their daily lives with one or more potentially serious health conditions. This reinforces the need for screening and referral services and it is noted that the unit cost of the screenings approximate $40.00 per participant over time. Health organizations, at times, have deemphasized the value of screening services. Rationale has included that screening without intervention does not lead to health status improvement. Because this approach includes screening, referral and follow-up, it insures that patients will become motivated to seek treatment. It is recommended that these screenings continue and from a public health perspective, should, over time, begin to reduce the numbers entering into CKD.

KIDNEY FUNCTION, OXIDIZED LDL AND CARDIOVASCULAR DISEASE (CVD)

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Oxidative stress has been implicated in CVD. The aim of this analysis is to assess whether oxidized low density lipoprotein (oxLDL) mediates the association of kidney function with CVD.

Study participants (N=2920) were older adults participating in the Health, Aging, and Body Composition study (Health ABC) recruited in Memphis, TN, and Pittsburgh, PA. Kidney function was assessed using eGFR and cystatin C. The oxLDL/LDL cholesterol ratio (%) was used as a surrogate of oxidative stress and lipoprotein peroxidation. CVD was defined as history of revascularization, myocardial infarction, or angina and taking antianginal medicines. Logistic regression was used to determine the association of oxLDL/LDL and kidney function with prevalent CVD.

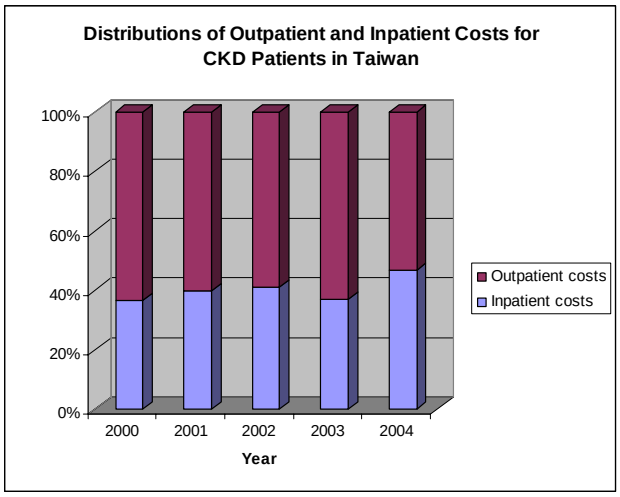
The mean age of participants was 74, cystatin C 1.0 g/L, eGFR 72.8 (21% with eGFR <60 ml/min/1.73m2), oxLDL/LDL 1.09 (range 0.08-6.0%); 51% were women, 41% black, 15% had diabetes. Linear regression revealed that cystatin C predicts oxLDL/LDL ratio ($p< 0.001$) after adjusting for age, race, gender, blood pressure, smoking, and diabetes. EGFR <60 was not associated with oxLDL/LDL ($p=0.89$), but there was trend for GFR <45 ($p=0.09$). OxLDL/LDL was associated with CVD after adjustment for age, race, gender (OR 1.25, (95% CI 1.04,1.49), $p=0.01$). After further adjustment for HDL, diabetes, blood pressure and smoking, the relationship was no longer significant (OR 1.14, (0.95,1.37), $p=0.16$). Both cystatin C (OR 1.23 per standard deviation, (1.12, 1.35) and eGFR <60 (OR 1.48, (1.19, 1.85) were associated with CVD, after adjustment. The addition of oxLDL/LDL did not attenuate the relationship for cystatin C or eGFR.

Decreased kidney function is associated with higher levels of oxidized LDL. However, this does not appear to mediate the association of kidney function with prevalent CVD.

LONGITUDINAL COST ANALYSIS OF CHRONIC KIDNEY PATIENTS IN TAIWAN

Lih-Wen Mau, Herng-Chia Chiu, Shang-Jyh Hwang, Allan J. Collins, Robert N. Foley. Unites States Renal Data System Coordinating Center, Minneapolis Medical Research Foundation, Minneapolis, Minnesota, USA. Kaohsiung Medical University, Kaohsiung, Taiwan

Not many studies have explored chronic kidney disease (CKD) costs in Taiwan, though CKD has become a global public health issue. The present longitudinal cost analysis of CKD in Taiwan was intended to examine medical services utilization by CKD patient characteristics and comorbid conditions. The study design was a retrospective secondary data analysis based on a 1% randomized sample of the National Health Insurance (NHI) claims data in Taiwan. From 2000 to 2004, the CKD patients accounted for 3.9% to 4.3% of total NHI annual expenditures; about 40% of the total CKD costs were spent on hospitalization (as shown in the following figure).Those aged 45 to 64 years had the highest share of total CKD costs. Those CKD patients with hypertension accounted for more than 50% of CKD costs annually. Although the current findings are descriptive, they can serve as a solid basis for further cross-national comparison of CKD costs.



TRAANSPLANATION HOSPITALIZATION AND QUALITY OF CARE FOR ESRD PATIENTS IN TAIWAN FROM 1996-2004

Lih-Wen Mau, Yao-Min Hung, Shang-Jyh Hwang, Herng-Chia Chiu, Allan J. Collins, Robert N. Foley. Unites States Renal Data System Coordinating Center, Minneapolis Medical Research Foundation, Minneapolis, Minnesota, USA. Kaohsiung Medical University, Kaohsiung, Taiwan

Taiwan has the highest incidence of end-stage renal disease (ESRD) world-wide, as reported by the United States Renal Data System. This study examined length of stay of transplantation hospitalization and associated medical costs and quality of care for kidney transplants in Taiwan.

Based on the claims data from the Bureau of National Health Insurance, 1,310 ESRD patients receiving kidney transplants from 1996 to 2004 were studied. Measurement of transplantation hospitalization focused on length of stay and associated total costs incurred during transplantation surgery.

In-hospital mortality and 14- and 30-day readmissions were indictors of quality of care. Mean age was 38.2 years (SD, 11.7) for the transplant sample. Average length of stay for transplantation surgery was 18.8 days. Total hospitalization costs averaged NT$ 227,514 (about US$ 7,198). The in-hospital mortality rate was 2.6%; re-admission rates were 9.3% within 14 days of discharge and 16.3% within 30 days. Significant risk factors of longer hospital stays and higher inpatient costs for transplantation surgery included diabetes, cardiovascular disease, infection, and rejection ($P < 0.05$). For adverse outcomes of transplantation, cerebrovascular disease, cardiovascular disease, and rejection were significantly associated with higher probability of in-hospital mortality ($P < 0.05$). The transplants with infection problems had an adjusted odds ratio of 1.82 for 30-day readmissions.

The current findings confirm significant associations between comorbid conditions and higher inpatient service utilization of kidney transplants, which supports the importance of clinical requirements for transplant candidates. The risk probability of in-hospital mortality and readmission of kidney transplants could be reduced by the management of hospital infection and acute rejection.

PREVALENCE OF ACE INHIBITOR AND ARB EXPOSURE IN ACUTE KIDNEY INJURY IN A TERTIRY REFERRAL CENTRE

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This study was undertaken to describe the prevalence of angiotensin converting enzyme inhibitor (ACEI) and angiotensin receptor blocker (ARB) exposure in cases of acute kidney injury referred to a Nephrology service in a tertiary referral centre.

Between July 1st 2006 and November 30th 2006 all referrals were prospectively evaluated. Age, sex, medication exposure, diabetic status, laboratory results and episodes of acute kidney injury were recorded. The Consultant Nephrologist decided whether the exposure of ACEI or ARB was contributory to the acute kidney injury episode.

During this period a total of 79 consultations were received, 28 males and 51 females. Mean patient age was 65.9 years. Twenty-three were classified as acute kidney injury. Of these, four had diabetes mellitus; the median admission and peak creatinine values were 139μmol/L and 349μmol/L respectively. Twenty-five patients were classified as having acute kidney injury on chronic kidney disease. Of these, nine were diabetic; the median admission and peak creatinine values were 247μmol/L and 373μmol/L respectively. Of the 23 patients with acute kidney injury, 8 were on an ACEI or ARB and 2 were on non-steroidal anti-inflammatory medications (NSAIDs). Of the 25 patients with acute on chronic kidney disease, 13 were on an ACEI or ARB and 4 were on NSAIDs. Thus, a total of 21 cases were exposed to ACEI or ARB in a setting where these medications were considered contributory to the episode of acute kidney injury.

ACEI and ARB exposure is an extremely common cause of acute kidney injury leading to Nephrology referral in a hospital setting. The data presented is likely grossly underestimated given the study design. The true economic cost of ACEI/ARB administration in such a population needs to take into account the cost of associated episodes of acute kidney injury.

PATIENT EXPERIENCE OF CHRONIC KIDNEY DISEASE (CKD): RESULTS OF A FOCUS GROUP STUDY

Michelle M. Richardson[1], Renee N. Saris-Baglama[2], Milena D. Anatchkova[2], Lesley A. Stevens[1], Dana C. Miskulin[1], Diane M. Turner-Bowker[2], Klemens B. Meyer[1], John E. Ware[2]. [1]Tufts-New England Medical Center, Boston, MA, USA; [2] QualityMetric Incorporated, Lincoln, RI, USA.

The aim of this focus group study was to identify the most important health-related quality of life (HRQOL) issues for patients with CKD as a first step in developing a computerized adaptive testing (CAT) system to assess HRQOL in patients with CKD (CKD-CAT).

CKD patients in Stages 3-5 not on dialysis (n=20) and Stage 5 on dialysis (n=20) were recruited from Boston-area clinics and dialysis units and interviewed in four focus groups separated by gender. Participants [52.5% men; 60% white, 30% African-American; 47.5% aged 45-64 years] defined “quality of life”, discussed the impact of CKD, and responded to sample HRQOL items. Sessions were audio taped and transcribed. Qualitative content analyses were conducted.

Participants defined “quality of life” as the way their lives were before CKD diagnosis, living a healthy and “normal” life, independence, and freedom. In rank order, patients identified mental health, intimacy/sexuality, fatigue, role functioning related to work, social relationships/support, independence, and finances as important areas affected by CKD.

When responding to sample HRQOL items that asked a patient to think about their kidney disease (e.g., In the past 4 weeks, how much of the time has your kidney disease left you too tired to do work or daily activities?), patients with CKD not on dialysis questioned whether they should focus on the disease itself or on the disease and its treatment. However, dialysis patients did not typically distinguish between the disease and its treatment.

Focus groups identified core areas affected by CKD and variations in item interpretation that require empirical testing. These findings will inform the development of a comprehensive HRQOL assessment, CKD-CAT, for this population.

AN ANALYSIS OF DARBEPOETIN DOSING PATTERNS FOR TREATMENT OF ANEMIA AT A LONGTERM ACUTE CARE HOSPITAL SETTING.

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Anemia of chronic disease is highly prevalent among survivors of critical illness and most of these patients are transferred to long-term acute care (LTAC) hospitals for further medical management. To date there is no data available regarding treatment of anemia of chronic disease in these patients. Our goal was to document the prevalence of anemia in this population and examine the practice patterns.

A retrospective study of long term acute care (LTAC) hospital patients (n=185) was undertaken. Variables included demographics; history of chronic kidney disease, diabetes, CHF, sepsis, acute renal failure, mechanical ventilation support, metabolic acidosis, hemodialysis dependency and number of dialysis sessions; admission hemoglobin; GFR ; number of packed red blood cell units; use of iron supplementation and darbepoetin dose (per kg/ day). Bivariate analysis compared each variable against change in hemoglobin (from admission to discharge). A statistical multivariate regression model for change in hemoglobin was also computed.

Sixty percent of LTAC patients exhibited improvement in hemoglobin values from admission. Twenty percent of patients receiving darbepoetin were dosed below recommended dosing guidelines (0.75mcg/kg). In bivariate analysis, only the number of units transfused ($r = 0.177$, $p = 0.017$), chronic kidney disease ($r = 0.173$, $p = 0.019$), CHF history ($r = -0.139$, $p = 0.059$) and admission hemoglobin ($r = -0.666$, $p < 0.001$) were associated with change in hemoglobin from admission. None of the remaining variables were associated with change in hemoglobin values from baseline. In multivariate analysis, only admission hemoglobin and history of chronic renal disease were independently associated with change in heme response (Model $R = 0.662$, ANOVA $F = 68.94$, $p < 0.001$).

Our retrospective analysis suggests that, especially in CKD patients, with adequate dosing and iron levels, improvements in anemia management can be achieved. Prospective trials are needed to study the efficacy of these protocols in this patient population.

HEALTH-RELATED QUALITY OF LIFE CONCEPTS MEASURED IN CHRONIC KIDNEY DISEASE RESEARCH

Renee N. Saris-Baglama[1], Alice L. Taubes[2], Michelle M. Richardson[2], Milena D. Anatchkova[1], Diane M. Turner-Bowker[1], Lesley A. Stevens[2], Dana C. Miskulin[2], John E. Ware[1], Klemens B. Meyer[2]. [1]QualityMetric Incorporated, Lincoln, RI, USA; [2]Tufts-New England Medical Center, Boston, MA, USA.

The study objectives were to identify patient-reported outcome measures used in chronic kidney disease (CKD) research and evaluate the comprehensiveness of covered concepts prior to developing a computerized adaptive testing system to measure health-related quality of life (HRQOL) in CKD patients (CKD-CAT).

A MEDLINE search using keyword terms (e.g., quality of life or health status and end-stage renal disease or chronic kidney disease) was conducted in May 2006, resulting in 2700 abstracts. Articles were reviewed if they contained a self-administered HRQOL tool, excluding measures of symptoms or patient satisfaction. Citations from review articles identified during the search were used to gather additional measures that were not identified by the initial search. Additionally, a supplemental MEDLINE search using new MESH terms identified from our first search was completed.

In the selected articles, we identified 115 generic and 19 disease-specific tools. The most widely used generic and disease-specific measures in CKD research were the SF-36® Health Survey and the KDQOL™, respectively. The most commonly assessed concepts across all tools included: Mental Health, Physical Functioning, Pain, Fatigue, and Social Functioning.

Results of this evaluation combined with information gathered through focus groups with CKD patients will inform the development of CKD-CAT, a comprehensive assessment tool for HRQOL measurement in this population.

SCREENING FOR CHRONIC KIDNEY DISEASE IN HUMAN IMMUNODEFICIENCY VIRUS

James Hall[1], Nahid Islam[1], Tibor Fulop[1], Leandro Mena[2], Harold Henderson[2], and Darren Schmidt[1].
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In June of 2006, the Infectious Disease Society of America released guidelines advocating screening for Chronic Kidney Disease (CKD) in patients with HIV. As a result, we started a screening program in our infectious disease clinic servicing a large HIV population in October 2005. We conducted a chart review to assess the efficacy of the screening program.

The screening program consisted of a routine urinalysis for protein and a serum creatinine (Cr). The abbreviated MDRD equation was used to estimate GFR. Chart review was conducted to determine the number of positive screens. Pearson Chi Square analysis was used to test for associations between subject characteristics and either proteinuria or GFR < 90 ml/min/1.73m2. Associations were considered statistically significant for $p < 0.05$.

Of the 931 charts reviewed, 707 had been seen during the past year. Of these 541 were screened for CKD. The mean age of the screened patients was 40.1 years (S.D.±10.1). They were 88.4% African American and 59.1% male. Most subjects (68.9%) were on HAART. Viral load (VL) was < 400 in 53.7%. CD4 was < 200 in 31.7%. Co-morbidities were common, diabetes (DM) in 9.6% and hypertension (HTN) in 32.2%. 12.6% had 1+ or greater protein per urine dipstick. DM, HTN, VL <400 and CD 4 < 200 were statistically associated with proteinuria, but African American ethnicity (AA) and absence of HAART therapy were not. 3.9% has a Cr > 1.4mg/dL. 33% had a GFR of less than 90 ml/min/1.73m2. HTN, DM, VL < 400, AA and the absence of HAART were associated with having an eGFR <90 ml/min/1.73m2, CD4 < 200 was not. **14% of charts met NKF criteria for CKD.**

CKD Stage	n	%
IV or V	4	0.7%
III	19	3.5%
II	13	2.4%
I	40	7.4%

CKD is common and screening seems justified in our HIV population

TRENDS IN MANAGEMENT OF CKD-RELATED ANEMIA IN THE VETERANS HEALTH ADMINISTRATION (VHA).

S L Seliger,[1] VD Hsu,[2] L Walker,[2] JC Fink[1]; Nephrology, U Maryland School of Medicine, Baltimore, USA[1]; Pharmaceutical Health Research Computing, U Maryland School of Pharmacy, Baltimore, USA[2].

The aim of this study was to identify trends in the prevalence and management of anemia among veterans with CKD. Active outpatients in the VHA with incident CKD were identified by a first estimated GFR <60cc/min/1.73m^2 within three 12-month periods before and after the release of national CKD care guidelines. Anemia was defined by an average Hb <13 g/dL (and < 11 g/dl) over a 6 month-period subsequent to the first low eGFR (all veterans were alive for the 6 month period). Nearly 25% of those with incident CKD in each year were not screened for anemia. Among those with anemia, roughly 40% did not have repeated testing of Hb with a declining proportion having repeat testing over time. A significant proportion of veterans with CKD and anemia received a blood transfusion; but, this declined over the time. Conversely, the proportion of veterans with CKD and anemia referred to Nephrology was also low but declined over time. All trends were significant (p <0.001).

Characteristic	**4/00 - 3/01**	**4/02 - 3/03**	**4/04 – 3/05**
Number with incident CKD	248,100	174,405	158,106
% with Hb measured	75.6%	76.4%	76.4%
Outpatient Hb <13 g/dl[1]	26%	25.5%	26.9%
% with repeat Hb testing[2]	62.7%	57.8%	56.6%
RBC transfusion[2]	7.7%	6.9%	6.9%
Nephrology specialty care[2]	5.9%	4.3%	4.0%
Outpatient Hb < 11 g/dl	5%	4.8%	5.3%
% with repeat Hb testing[2]	72.8%	67.9%	66.5%
RBC transfusion[2]	22.9%	20.8%	19.7%
Nephrology specialty care[2]	10.7%	7.0%	6.4%

1) Among those with Hb measured; 2) Among those with anemia as defined

Anemia is prevalent among veterans with CKD but there appears to be little impact of national CKD guidelines for evaluation and treatment of anemia at the current time. Strategies are needed to facilitate dissemination of practice guidelines for CKD in health networks such as the VHA.

A CROSS SECTIONAL STUDY OF COMPLIANCE WITH K/DOQI CLINICAL PRACTICE GUIDELINES FOR CHRONIC KIDNEY DISEASE IN AN URBAN TEACHING CLINIC.

Shahzad Shafique; University of Connecticut, Farmington, USA.

Background: The objective of the study was to determine the compliance of residents with K/DOQI clinical practice guidelines in a teaching clinic and to generate a novel strategy to improve it.
Methods: We performed a cross-sectional analysis of 83 patients with diagnosis of CKD for the period "Jan 2005-Dec 2005". The charts were reviewed to determine whether K/DOQI goals were met for: 1) assigning stage of CKD and estimation of GFR, 2) assessment of proteinuria, 3) BP control, 4) evaluation of metabolic bone disease by Ca, PO4, and PTH measurement, 5) lipids management, 6) timely nephrology referral, 7) interventions to slow the progression of the disease, and 8) evaluation and treatment of anemia, and nutritional status.
Results: In these 83 patients the mean Scr was 1.9 mg/dl, and eGFR was 38.3 ml/min. We found failure to assign the stage of the disease in 71 (86%). Proteinuria was assessed in 23 (28%) of all. Among 73 (88%) patients with recorded history of HTN only 28 (38%) showed optimal control. 25 (30%) were anemic but evaluation of anemia was done only in 7 (28%). Nutritional status was assessed only in 9 (11%) and no one was referred to a dietician. The work-up for evaluation of metabolic bone disease was frequently missing: PTH levels were obtained in only 3 (3.6%) and Ca in 19 (23%) and PO4 in 15 (18%). Lipid profile was ordered in 58 (69%) and found to be abnormal in 74%. The nephrology referral was initiated only in 17 (20%) patients.
Conclusion: The study concluded that K/DOQI goals are achieved in only a small proportion of patients cared for in a teaching clinic. The breadth of the problem suggests that both systematic and educational barriers impair translation of K/DOQI guidelines into clinical practice and to achieve optimal disease specific management outcomes. On the basis of this study "Kidney Early Evaluation and Protection" (KEEP) flow sheets were successfully introduced to increase the compliance rate with the above guidelines.

HYPOALBUMINAEMIA – A MARKER OF CARDIOVASCULAR DISEASE IN PATIENTS WITH CHRONIC KIDNEY DISEASE STAGES II - IV

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Cardiovascular disease (CVD) is a major cause of morbidity and mortality in patients with chronic kidney disease (CKD) patients. Serum albumin, a negative acute-phase reactant and marker for underlying inflammation and/or malnutrition, is an independent predictor of CVD and mortality in CKD VI patients. Such an association in patients with less severe CKD is not well established.

We conducted a cross sectional study of all CKD II - IV patients attending the nephrology clinic (N=376; mean age: 57±17 years; GFR: 47±20 mL/min/1.73m2; females 48%; blacks 15%; diabetics 27%; hypertensive 79%). Laboratory and clinical data including risk factors and evidence of CVD were obtained at the point of the most recent visit. The association between risk factors and CVD was evaluated by logistic regression. In the simple logistic regression model, age ($p<0.0001$), sex ($P=.0.02$), hypertension ($P<0.0001$), diabetes ($P<.0001$), dyslipidemia ($p=.01$), and serum albumin ($p<.0001$) were found to be statistically significant. Serum albumin was found to be an independent predictor ($p=0.002$) of CVD by multiple logistic regression analysis using the above risk factor variables.

In conclusion: a) hypoalbuminaemia is an independent predictor of CVD in early CKD stages; b) hypoalbuminaemia may be used to identify the population at higher risk for CVD.

COMORBIDITIES AMONG PATIENTS WITH CHRONIC KIDNEY DISEASE.

David Simon[1], Fredric Finkelstein[1], Beth Barber[2], Louis Matza[3], Rohit Borker[2], Karen Malley[3]. 1. Metabolism Associates, P.C., New Haven, CT, USA. 2. Amgen, Inc., Thousand Oaks, CA, USA. 3. United BioSource, Corp., Bethesda, MD, USA. An estimated 20 million patients suffer from chronic kidney disease (CKD) in the United States. Often, these patients are also diagnosed with comorbidities that add to the high clinical and economic treatment costs associated with the disease as it progresses. This research explored the comorbidities among patients with CKD stages 3, 4 and 5. The analysis was performed with data from a large nephrology practice from the Northeast. Patients had at least one visit to the practice between July 1, 2004 and June 30, 2006. Stage of kidney disease was determined based on the patient's first eGFR value using the MDRD equation. Patients were excluded if they had dialysis prior to their first eGFR. A total of 1,886 patients were identified as having CKD stage 3, stage 4 or stage 5 (n=1,074, n=635, and n=177, respectively). The average age of the total sample was 69.4 (SD=13.9) years, 53.2% were male, 83.6% were Caucasian, and 13.4% were African American. There were substantial comorbidities among all stages of CKD (Table). There appears to be a somewhat larger percentage of patients with CHF in stages 4 and 5 compared to stage 3, nonetheless, the percentage of patients with stage 3 who have CHF is considerable. Most comorbidities among patients with stages 3 and 4 are just as high as that of patients with stage 5, suggesting significant burden occurs early in the disease progression.

Table: Comorbidities Among Patients with CKD

Comorbidities	Stage 3	Stage 4	Stage 5
Diabetes Mellitus %	42.7	46.5	45.8
Hyperlipidemia %	71.7	73.1	72.9
Coronary Artery Disease %	25.9	30.7	26.0
Congestive Heart Failure %	13.8	25.2	20.3
Myocardial Infarction %	4.7	5.0	5.6
Hypertension %	72.7	77.2	73.4
Peripheral Vascular Disease %	9.1	14.5	9.0
Other Cardiovascular Disease %	6.2	6.3	4.0

CONSISTENT IN-TARGET HEMOGLOBIN OVER THE TRANSITION TO DIALYSIS: EFFECT ON OUTCOMES

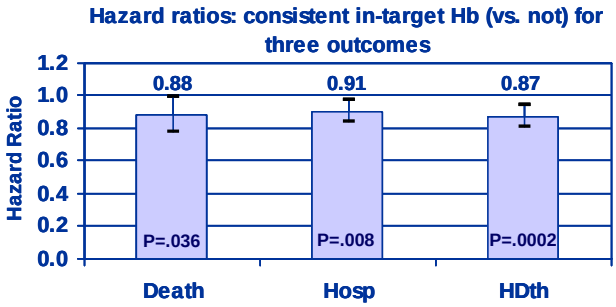
Melissa Skeans[1], Tom Arneson[1], Stephan Dunning[1], Michael del Aguila[2], David Gilbertson[1], Allan Collins[1]. [1]Chronic Disease Research Group, Minneapolis Medical Research Foundation, Minneapolis, Minnesota, USA. [2]Roche Laboratories Inc., Nutley, New Jersey, USA

Maintaining stable hemoglobin (Hb) throughout the progression from CKD stage 4 to 5 is important to the care of anemic patients. We studied maintaining consistent in target Hb levels with hospitalization (Hosp), mortality, and a composite endpoint of hospitalization or death (HDth).

Our cohort included 7069 dialysis patients aged 67 years or older, incident from January 1, 1998, to September 30, 2003, with ESA claims over the transition from 3 months before dialysis initiation to 3 months after. In-target patients (22%) consistently maintained in-target Hb levels, 10-12 g/dL through initiation and 11-12.5 g/dL 3 months after initiation. Patients were followed 1 year after transition. Kaplan-Meier methods were used to compare unadjusted 1-year outcomes by target status. Cox models were used to compare target status effect, adjusted for factors documented to be associated with consistently in-target Hb levels such as measures of comorbidity and disease severity.

Patients consistently in-target had lower unadjusted rates of all 3 outcomes: 21.8% vs. 24.4% (death), 58.0% vs. 61.8% (Hosp), and 61.7% vs. 66.5% (HDth). Adjusted for potential confounders, in-target patients had better outcomes vs. those not in-target.

Consistently maintaining in-target Hb levels across the transition to dialysis reduces hospitalization and mortality.



ASSOCIATION BETWEEN MORTALITY AND MODALITY IN THE FIRST 90 DAYS FOLLOWING INITIATION OF DIALYSIS.

Jon Snyder, Yi Peng, Eric Weinhandl, David Gilbertson, Tom Arneson, Allan Collins, Chronic Disease Research Group, Minneapolis, MN.

Studies of mortality comparing hemodialysis (HD) with peritoneal dialysis (PD) in the US have typically initiated patient follow-up on day 90 of therapy. Questions therefore arise as to what happens during the first 90 days. We studied the mortality experience of PD and in-center HD patients over the first 90 days of therapy for patients initiating therapy between 1995 and 2004 (N=799,187). Initial dialysis modality was determined from the 2728 form designation at the initiation of therapy. All-cause mortality was assessed through day 90. Patients were censored at transplantation or 60 days following a switch in dialysis modality. Adjusted hazard ratios for mortality are shown in the table, stratified by diabetic status and the presence of baseline comorbidity on the 2728 form.

Diabetic (DM) Status	Baseline Comorbid Conditions	Hazard Ratio (PD:HD)	95% Confidence Interval
Non-DM	None	0.44	0.40-0.49
	One or more	0.73	0.68-0.78
DM	None	0.49	0.43-0.56
	One or more	0.75	0.70-0.80

Hazard ratios were estimated from a Cox proportional hazards model with adjustment for year of initiation, age, gender, race, body mass index, baseline eGFR, hemoglobin, and serum albumin. We conclude that patients who initiated therapy on PD are approximately 50% less likely to die during the first 90 days of therapy compared with in-center HD patients when no comorbidities are listed at the time of initiation. For patients with at least 1 comorbidity, the risk is approximately 25% less. While causal conclusions cannot be made from this analysis, further investigation of the first 90 days for patients chosen to be on PD vs. HD could elucidate differences between the populations.

THE ASSOCIATION OF PERSISTENTLY LOW HEMOGLOBIN LEVELS WITH HOSPITALIZATION AND MORTALITY, Craig A Solid, Eric Weinhandl, David T Gilbertson, Allan J Collins. Chronic Disease Research Group, Minneapolis, MN.

Examining the association between persistently low hemoglobin (Hb) levels (< 11.0 g/dL) and outcomes such as hospitalization or mortality is complicated by changing status of comorbidity, disease severity and other intercurrent events. This study employed a marginal structural model (MSM) to account for changing patient status.

We identified incident hemodialysis (HD) patients during 2002, and followed them forward for up to two years. To be included patients had to have Medicare as their primary payor, remain on HD and have valid erythropoietin claims (to be able to obtain hemoglobin level). In addition to demographic information and the type of dialysis unit, we used Medicare claims to identify comorbid conditions, hospital days, and elements of care such as Vitamin D use and blood transfusions. We then employed a History-Adjusted MSM to find associations with subsequent hospitalization and mortality.

A total of 54,328 patients met the inclusion criteria and eligible for analysis. The results of the MSM demonstrated a significant increase in mortality as the length of time with a Hb < 11 g/dL persisted. During a rolling 3-month follow-up period, patients were classified as having a Hb < 11 for 0, 1, 2 or 3 months. The adjusted odds ratios for mortality and hospitalization are as follows:

	Hospitalization		Mortality	
	Odds Ratio	95% CI	Odds Ratio	95% CI
0 Months	Reference		Reference	
1 Month	1.29	(1.27, 1.32)	1.36	(1.28, 1.44)
2 Months	1.42	(1.38, 1.46)	1.72	(1.60, 1.84)
3 Months	1.70	(1.63, 1.76)	2.48	(1.28, 1.44)

The risk of hospitalization and mortality increases significantly with each additional month patients spend below the target Hb range.

THE EFFECT OF HYPONATREMIA ON THE SAFETY AND EFFICACY OF NESIRITIDE

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BACKGROUND: The interaction between vasoactive therapy and serum sodium is well known. Nesiritide, when used in acute decompensated heart failure, occasionally decreases serum sodium. Whether pre-existing renal dysfunction alters the efficacy and safety of this drug is unknown.This study assessed the hypothesis that pre-existing renal dysfunction does not alter the safety and efficacy of nesiritide.

METHODS: Data were collected on 183 consecutive patients who were admitted to our hospital, enrolled in the ADHERE registry (Acute Decompensated Heart Failure National Registry) and received nesiritide. The data were abstracted with a prespecified data collection sheet from a combination of patient charts and the ADHERE database. Measured serum sodium was used to classify patients into tertiles of natremia and also as a continuous variable. Improvements in Cardiac Index(CI), Systemic Vascular Resistance(SVR), Thoracic Fluid Content(TFC), symptoms and Length of Stay(LOS) were used as efficacy variables. Hypotension and ventricular arrhythmias were the safety variables.

ANALYSIS: Chi-square was used to determine differences in distribution of categorical outcome variables. ANOVA was used to determine differences in means of continuous outcome variables. Regression analysis and a General effects model were used to determine if baseline differences between the groups had any confounding effect on the results.

RESULTS: In the sample, 52% were men, 76% were caucasian and their mean age was 72 years. No significant difference was found between different sodium groups with respect to any of the safety or efficacy variables. Secondary analysis of different sub-groups with respect to possible confounders revealed no effect on primary result.

CONCLUSION: This study did not reveal any effect of baseline serum sodium on the safety or efficacy of nesiritide when administered to patients with acute decompensated heart failure.

ALBUMINURIA AND AGE AS PREDICOTRS OF ERYTHROPOIETIN RESPONSE IN CHRONIC KIDNEY DISEASE

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Resistance to epoietin alpha (EPO) in patients with chronic kidney disease (CKD) has been associated with severe secondary hyperparathyroidism, iron deficiency, medications, and chronic inflammation. There is mounting interest in the metabolic dysregulation seen in CKD patients with Metabolic Syndrome with resultant chronic inflammation as another component of EPO resistance. Recent evidence supports hypertension and albuminuria (components of the metabolic syndrome) as possible modulators of EPO resistance. To investigate the metabolic influence on EPO resistance, we retrospectively collected data on 65 predominantly Caucasian male patients with CKD being treated with recombinant EPO. Erythropoietin resistance index (ERI) was defined as the weekly epoietin dose divided by hemoglobin divided by body weight in kg. Non-parametric correlation testing was used to assess significant relationships between ERI and other variables. Significant correlations were found between ERI and age ($r=0.281$, $p<0.0001$), urine protein/creatinine ratio ($r=0.301$, $p=0.001$), serum transferrin saturation ($r=-0.222$, $p=0.003$), serum albumin level ($r=-.300$, $p<.0001$) and serum intact PTH ($r=0.157$, $p=0.012$). There were no significant correlations between ERI and serum ferritin level, estimated glomerular filtration rate, mean arterial pressure, systolic blood pressure, or diastolic blood pressure. Multivariate analysis revealed that age (beta = .305) and serum albumin level (beta = -.247) were the only independent variables predicting ERI. Serum albumin varied inversely with urine protein/creatinine ratio ($r=-.430$, $p < .0001$) and positively with serum hemoglobin level ($r=.300$, $p < .0001$). Use of statin, ace inhibitor, or angiotensin II receptor blocker did not affect erythropoietin responsiveness in this group. Age, proteinuria, and hypoalbuminemia are associated with decreased EPO responsiveness.

SHORT-TERM SURVIVAL EFFECT OF EARLY NEPHROLOGY CARE PRIOR TO DIALYSIS INITIATION IN ELDERLY PATIENTS WITH END-STAGE RENAL DISEASE

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The survival effect of early nephrology care prior to dialysis initiation is still controversial. The research objectives were to reexamine if early nephrology care prior to dialysis initiation is associated with improved 6-month dialysis survival rate and also to assess whether greater use of early nephrology care would be expected to improve the short-term survival for the patients defined by instrumental variables (IVs).

Methods: The research subjects were patients who aged 67+ years at hemodialysis initiation in 1996-1999 and had Medicare Part A and B fee-for-service coverage for 2 years prior to dialysis initiation. Major data sources were CMS Form 2728 data, Modality Sequence files, and Medicare claims, which were used to develop early nephrology care defined as seeing a nephrologist between 24 and 13 months and between 12 and 4 months prior to dialysis initiation as well as late nephrology care defined as visiting a nephrologist within 3 months prior to dialysis initiation. Three IVs, which were access-related variables, were generated from U.S. 2000 Census data and claims data.

Results: About 23.53% of 70,905 elderly patients died in 6 months after initiating hemodialysis. After controlling patient demographics, comorbidities, non-nephrologist physician visits and other covariates, traditional logistic regression showed that patients who received early and late nephrology care had greater odds ratios of surviving in the 6 months of dialysis. However, IVs regression models showed no significant survival benefits in the 6 months of dialysis among the patients whose selection of early and late nephrology care was significantly affected by the 3 IVs.

Conclusions: Elderly patients who received early nephrology care appear to have better 6-month survival rates as previously reported. However, our IV results suggest that this improved outcome may be due to residual uncorrected confounding variables, and that increasing the fraction of patients receiving early nephrology care may not significantly improve 6-month survival rates.

PREVALENCE OF CHRONIC KIDNEY DISEASE (CKD) IN PATIENTS REFERRED TO A HEMATOLOGIST FOR ANEMIA: AN EPIDEMIC PROBLEM

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Despite a high prevalence of CKD (NHANES general population estimate: overall, 11%; >65 years, 25%) and a strong association of CKD with anemia, many patients referred to a hematologist for anemia evaluation frequently have a CKD diagnosis overlooked. The hypothesis of this study was that patients referred to a hematologist for evaluation of anemia represent a population enriched with CKD.

A retrospective chart audit was performed (01Jan2004 to 31Dec2005) on all patients being referred by community physicians to a hematology practice for the evaluation of anemia. Patients with known CKD, malignancy, and/or myelodysplastic process were excluded.

The cohort consisted of 256 patients (male, 37.5%; female, 62.5%; mean age, 67.6 ± 15.9 years). Mean hemoglobin (Hb) was 10.3 ± 1.87 mg/dL. Mean serum creatinine (SCr) was 1.16 ± 0.74 mg/dL, with a mean eGFR (modified MDRD, 4-variable equation) of 69.9±34.2 ml/min/1.73 m^2. Despite having what most clinicians would perceive as a normal SCr level, approximately one third of patients already had stage 3 CKD.

	N	%	Mean GFR ± SD (mL/min/1.72 m^2)	SCr ± SD (mg/dL)
GFR > 90 (1)*	51	19.9	116.7 ± 40.3	0.7 ± 0.1
GFR 89 – 60 (2)	97	37.9	75.7 ± 9.1	0.9 ± 0.2
GFR 59 – 30 (3)	95	37.1	45.9 ± 7.9	1.4 ± 0.3
GFR 29 – 15 (4)	9	3.5	24.5 ± 4.6	2.3 ± 0.5
GFR < 15 (5)	4	1.6	11.2 ± 3.9	5.2 ± 2.9

*Number in parentheses = K/DOQI CKD stage

In conclusion, assuming a conservative definition of CKD as a GFR < 60, in the study cohort, 55.8% (n=87) of the patients > 65 years old with anemia also had CKD. This is more than double the NHANES estimated prevalence of 25%.

This information stresses the need to assess all anemia patients for CKD stage via eGFR calculation, especially given the synergistic effect of anemia and CKD on adverse clinical outcomes.

TREATMENT OF IDIOPATHIC MEMBRANOUS NEPHROPATHY (IMN) WITH THE CHINESE HERBAL *ASTRAGALUS MEMBRANACEOUS. (AM)*

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A 77-year-old woman presented in 7/02 with nephrotic syndrome and normal renal function. Renal biopsy revealed membranous nephropathy and workup for secondary causes was negative. Treatment with cyclosporin for 6 months followed by mycophenolate mofetil for 6 months did not induce a remission. She was also treated with ACE inhibitor/ARB combination. Despite these measures, she continued to have nephrotic-range proteinuria over a >2-year period. In 10/04, she sought treatment from a traditional Chinese physician, who administered a Chinese herbal medicine with the active ingredient *Astragalus membranaceous*. Within 4 months her proteinuria decreased from 9.5 g/g to 1.6 g/g (Table) and her edema resolved. After cessation of *AM* therapy on 2/1/05, her proteinuria increased from 1.6 g/g to 4.3 g/g within 6 weeks and she again became edematous. After reinitiation of therapy on 3/11/05, her proteinuria decreased to 1.7 g/g within 3 months. She was treated for 18 months as recommended by her traditional Chinese physician and is currently in complete remission with undetectable proteinuria. No side effects of the treatment were seen.

While it is possible that our patient may have undergone spontaneous remission, we believe this to be unlikely in view of the duration of nephrosis prior to treatment with *AM*, the recurrence of nephrotic syndrome after cessation of *AM*, and the complete remission of nephrosis after its reintroduction. The known immunomodulatory effects of *AM*, and its effects idiopathic membranous nephropathy are postulated, a disease for which there are few therapeutic options.

Start *AM* ⇓ Stop *AM* ⇓ Restart *AM* ⇓ Completed *AM* ⇓

Date	9/04	11/04	2/05	3/05	4/05	6/05	1/06	4/06
U Pr/Cr	9.5	8.3	1.6	4.3	4.0	1.7	0.12	<0.3
Serum albumin	2.4	2.6	2.8	2.7	3.3	N/A	3.2	3.8

ACUTE KIDNEY INJURY SECONDARY TO CLL ASSOCIATED GLOMERULONEPHRITIS AND CONCOMITANT RENAL INFILTRATION – A CASE REPORT.

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Cryoglobulinemic Glomerulonephritis (CGN) is a known but uncommon manifestation of chronic lymphocytic leukemia (CLL). Renal involvement is commonly seen in CLL, but acute kidney injury (AKI) due to leukemic infiltration is very rare. We present a rare case of AKI secondary to CLL associated CGN secondary to type I cryoglobulin and concomitant renal parenchymal invasion by CLL.

A 58-year-old female with a history of stage I CLL for several years presented with a chief complaint of lower extremity edema and 2.6 grams of protein in a 24hr urine collection. Her past medical history was significant for a biopsy proven cryoglobuinemic skin rash that had resolved several months prior. Labs showed a creatinine of 1.0 mg/dl and positive immunofixation of serum and urine for IgG lambda. Complements were normal. A biopsy was done and demonstrated diffuse proliferative glomerulonephritis consistent with CGN and renal parenchymal infiltration by CLL. Immunoflorescence showed a type I cryoglobulin. The patient was started on a chemotherapy regimen consisting of Fludarabine and Rituxan.

A follow up creatinine 1month later demonstrated a creatinine of 0.8mg/dl and protein/creatinine ratio of 0.2.

CGN has been associated with CLL but this is uncommon. To date there have been very few relevant reported cases. Our case is unique in that there is both CGN with type I cryoglobulin and concomitant renal parenchymal invasion by CLL causing AKI.

NOVEL ASSOCIATION OF MPGN WITH GRAVES' DISEASE

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A previously healthy 22 year old Caucasian male presented with one month of flu-like symptoms with progressive nausea and vomiting. He had been physically active and prior physical exams and urinalyses had been unremarkable. Initial laboratory values showed a BUN of 55 mg/dL (range 8-24) and Creatinine of 1.7 mg/dL (range 0.9-1.4). His blood pressure was 194/120 mmHg. A urinalysis revealed glomerular hematuria with RBC casts, a few leukocytes, numerous hyaline casts, and 1-3 renal epithelial cells per HPF. A 24 hour urine collection revealed 13.7 grams of proteinuria. HIV, Hepatitis serologies, ANA and anti-ds-DNA, ENA, cryoglobulins, SPEP, and ANCA were also negative. Total complement and C3 were low. A renal biopsy showed a type 1 MPGN. At the same time, a diagnosis of Graves' disease was made with free T3 9 pg/mL (range 2.3-4.21) and free T4 3.6 ng/dL (range 0.8-1.8). Anti-thyrotropin receptor antibody was markedly positive and anti-TPO antibody was negative. He received therapy for his Graves' disease including methylprednisolone, iodine, and propylthiouracil, and later 2 doses of radioactive iodine. His hypertension was controlled and the MPGN was treated conservatively with an ACE inhibitor. He is now doing well 16 months after presentation. Urinary sediment, serum creatinine, and protein excretion are normal; his antihypertensive medications are being tapered. The manifestations of MPGN (acute renal failure, hypertension, and proteinuria) resolved with conservative measures and treatment of the Graves' disease.

There are sporadic reports of thyroid conditions being associated with glomerular diseases. Both Graves' disease and Hashimoto's thyroiditis have been associated with membranous nephropathy. There are also cases of minimal change disease and ANCA glomerulonephritis in association with Hashimoto's thyroiditis. Hashimoto's thyroiditis has also been associated with MPGN and a crescentic glomerulonephritis. To our knowledge this is the first report of an MPGN associated with Graves' disease, and therapy directed at the Graves' disease may have aided in the recovery from the MPGN.

CLINICAL PREDICTORS OF SEVERITY OF PROTEINURIA IN A COHORT OF PATIENTS WITH HEPATITIS C AND PROTEINURIA. Susan M. Hailpern, Robin Arora, Salman Waheed, Belinda Jim, Anjali Acharya; Jacobi Medical Center and Albert Einstein College of Medicine; Bronx, NY USA

Glomerular disease with proteinuria and renal failure is seen in patients with hepatitis C infection (Hep-C). Hep-C has also been independently associated with microalbuminuria in the absence of diabetes. The purpose of this study was to examine the association of clinical and laboratory factors as well as co-morbid conditions on the degree of proteinuria in a cohort of Hep-C patients.

We performed a retrospective chart review of 239 patients with a primary diagnosis of Hep-C who may have also had other co-morbid conditions. Charts were reviewed for clinical and demographic characteristics. Proteinuria was dichotomized ≥100 mg. Continuous variables were compared between proteinuria groups using Student's t-tests; categorical variables were compared between proteinuria groups using chi-square tests. A multivariable logistic regression was used to examine the association between proteinuria ≥100 mg and clinical and demographic characteristics of the Hep-C patients.

The cohort was 38% male, mean age 51.2 years ± 8.9, with 44.4% having proteinuia ≥100mg. The proteinuria ≥100 mg group had a significantly lower hemoglobin, albumin, and total protein (p=0.01, 0.01, and 0.03, respectively). This group was less likely to have a prior diagnosis of hypertension (p=0.01). There were no statistically significant differences in the prevalence of diabetes (p=0.29), age (p=0.99), or sex (p=0.29) between the two groups. In multivariable logistic regression, albumin was significantly and *inversely* associated with proteinuria ≥100 mg (OR: 0.53; 95% CI: 0.36, 0.76), as was PT (OR: 0.87; 95% CI: 0.79, 0.95) and a prior diagnosis of hypertension (OR: 0.32; 95% CI: 0.13, 0.79).

In summary, among patients with Hep-C proteinuria ≥100 mg was independently and inversely associated with a history of hypertension albumin, and prothrombin time. This study found no association between proteinuria ≥100 mg and a history of diabetes or age. Further research is needed to explore the implications of these observations.

THE EFFECT OF COMBINATION TREATMENT WITH PEGYLATED INTERFERONα AND CYCLOSPORIN A ON MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS INDUCED BY HEPATITIS C VIRUS

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We describe the use of a combination of pegylated interferon-α2a (PEG-INFα-2a) plus cyclosporin A (CsA) to treat a patient with membranoproliferative glomerulonephritis (MPGN) induced by hepatitis C virus (HCV). A 62-year-old woman was diagnosed with chronic active C hepatitis in March 2005. PEG-IFNα-2a was subcutaneously administered at a dose of 90 μg every 2 weeks for 12 months. The drug was well tolerated by the patient. Her serum aminotransferase level normalized and HCV-RNA decreased but did not disappear. In early June, the patient had facial and leg edema, massive ascites and hypertension. She was diagnosed with nephrotic syndrome with renal dysfunction. Serological examination revealed cryogloblinemia, hypocomplementemia, an elevated rheumatoid factor level and increased HCV-RNA. We therefore suspected HCV-associated glomerulonephritis and started subcutaneous injection of PEG-INFα-2a at the same dose. Since urine protein (U-Pro) increased 2 weeks after the first PEG-INFα-2a injection, we continued PEG-INFα-2a and added oral CsA administration at a dose of 3 mg/kg/day, maintaining the patient's blood trough level at 100-150 ng/ml. U-Pro gradually decreased and finally disappeared without further serum creatinine elevation. Cryoglobulin did not disappear, but HCV-RNA (high-range method) decreased by less than 5 KIU/Ml. Massive ascites also disappeared, and we were thus able to perform renal biopsy, upon which immunofluorescence examination revealed MPGN with the deposition of IgG, IgM and C3 along the peripheral capillary wall. However, electron microscopy found no cryoglobulin deposition. The combination therapy of PEG-INFα and CsA may be an option for patients with MPGN associated with HCV.

MEMBRANOUS MEPHROPAHTY IN **ASSOCIATION WITH AUTOIMMUNE THYROIDITS AND UNEXPLAINED LEUKOPENIA – A NEW CLINICAL SYNDROME?**

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A 20 years old lady with Hashimotos thyroiditis was evaluated for leukopenia detected on routine laboratory testing. Bone marrow biopsy showed a hypercellular marrow and a normal female chromosome complement. After 3 years she developed nephrotic syndrome. Kidney biopsy showed membranous nephropathy. Her labs are Vitamin B12 479ng/L, Hepatitis B and C, RF, DNA (DS) Ab, Lupus anticoagulant, anti RNP Ab, Anti Sm Ab, RPR and HIV Ab were negative, ANA initially negative in 06/2000 then become weakly positive with a titer of 1:40 in 09/2003, Complement levels were normal, B2 microglobulin 1.5mg/L.

Autoimmune thyroiditis in relation to membranous nephropathy has seldom been reported and the exact mechanism relating the two diseases is unclear. It has been noted that thyroid antibodies are significantly higher in patients with autoimmune disease. But this patient has only tested weakly positive for ANA. The cause of the leucopenia remains unclear to date. This disease complex of autoimmune thyroiditis, membranous nephropathy and leucopenia has never been previously reported. We believe that this is of an autoimmune nature but the exact mechanism remains undetermined.

A CASE OF COLLAPSING FSGS ASSOCIATED WITH STILL'S DISEASE.

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Collapsing FSGS is commonly described in HIV patients, though many cases have been reported in non-HIV related diseases in the recent years. We present a rare case of collapsing FSGS in a patient with Still's disease. Case Presentation: A 43 y/o hispanic female with no significant past medical history presented with fevers and joint pains for 5 months. P/E revealed a temperature of 103.2 F, diffuse macular skin rash, axillary lymphadenopathy, hepatosplenomegaly, synovitis at the wrists and pedal edema. Labs revealed: WBC 18,000, 88% neutrophils, BUN/Creat 47/6.8, Ferritin 1650, reactive hyperplasia on lymph node biopsy, nephrotic range proteinuria of 8 gm/day, negative ANA and RF and negative viral, bacterial and fungal blood cultures. A detailed work up was negative for infection, malignancy, rheumatologic or autoimmune diseases. She was diagnosed with Adult Still's disease as per the Yamaguchi criteria. Renal biopsy results were consistent with the collapsing FSGS. She was started on Prednisone and all her systemic symptoms resolved with regression of her proteinuria from 8gm/day to 3 gm/day. Her renal function has remained stable for the past 18 months with a BUN/Creat of 42/4.0 with no dialysis requirements. Discussion: Non HIV related FSGS has been described in patients with Parvovirus B19 infection, autoimmune disorders, Hepatitis C viral infection and rarely in patients using Pamidronate; our patient had a negative workup for all of the above. In recent years, patients with Still's disease have been described to have proteinuria and hematuria, though very little has been elucidated in terms of histologic diagnosis. Collapsing FSGS is typically described as an aggressive variant of FSGS with rapid progression to end stage renal disease and poor response to treatment. Notably in our patient, the renal disease regressed parallel to the symptoms of Still's disease, which might point to a better prognosis, and hope of resolution in such cases. Also it suggests a common pathophysiology, possibly immune complex mediated, of the two conditions. Early recognition and intervention for glomerular involvement in Still's disease may thus help us better understand the disease mechanisms and the association between the two disease entities.

PROLIFERATIVE GLOMERULONEPHRITIS IN A PATIENT WITH ANGIOIMMUNOBLASTIC T CELL LYMPHOMA

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Angioimmunoblastic T cell lymphoma or angioimmunoblastic lymphadenopathy with dysproteinemia (AILD) is a type of peripheral T cell lymphoma, which accounts for only 1-2% of the non- Hodgkin's lymphomas. There have been a few case reports of renal manifestations related to AILD. We describe a case of proliferative glomerulonephritis without immune deposits in a case of angioimmunoblastic T cell lymphoma.

68-years-old male presented with weight loss, intermittent fevers of 3 months duration and generalized lymphadenopathy. He was diagnosed with AILD on lymph node biopsy. Subsequently, he developed acute renal failure with hematuria and nephrotic range of proteinuria. Examination of urine sediment revealed dysmorphic RBC, and random urine protein/ creatinine ratio was 4.1. Kidney biopsy revealed proliferative glomerulonephritis with increase in mesangial cellularity and endocapillary proliferation, and mild interstitial fibrosis. Immunoflorescence revealed focal 1+ C3 staining in the glomerular capillary walls and mesangium. There were no immune deposits on electron microscopy. As the renal function deteriorated, he required hemodialysis because of fluid overload, and received one cycle of chemotherapy (cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisone-CHOP regimen). Proteinuria and lymphadenopathy improved, but post chemotherapy course was complicated by neutropenic sepsis, and patient expired.

On review of the literature, most other cases of glomerulonephritis reported in AILD had immune deposits. In only one other case in addition to ours, had no immune deposits. In that case, patient had glomerulonephritis with crescents and IgM colonization of mesangium. He responded to chemotherapy and did not require renal replacement therapy. Our case did not have any crescents and there was no immunoglobulin staining. We postulate that probably cell mediated immune reaction and/ or alternate complement pathway activation (as evidenced by focal C3 staining) might have contributed to the glomerulonephritis in our case.

PODOCYTE INJURY OCCURS IN THE COURSE OF PREECLAMPSIA

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Preeclampsia remains one of the leading causes of maternal and fetal morbidity and mortality. Though the podocyte has not traditionally been thought to be involved in preeclampsia, conditional knock out mice of VEGF in the podocyte showed typical pathologic features of preeclampsia. Our hypothesis is that the podocyte is injured in the course of preeclampsia, contrary to previous reports. We studied the expression of podocyte-specific proteins, synaptopodin and podocin, by immunofluorescence, in renal biopsies of 20 preeclampsia patients within 4 weeks of delivery. These patients excreted urinary protein ranging from 2.2 to 15 g/day. All biopsies had some degree of endotheliosis, 6/20 biopsies showed segmental sclerosis. In 11/20 samples with severe endotheliosis, +/- sclerosis, podocin expression was markedly decreased, while synaptopodin expression was either unchanged or slightly decreased. The remaining 9/20 samples which had only mild endotheliosis, showed normal synaptopodin and podocin expression. Podocin appears to be first downregulated in severe endotheliosis, followed by decreased synaptopodin expression in the presence of segmental sclerosis. Podocyte injury correlates with the degree of endotheliosis and/or segmental sclerosis in preeclampsia. The histological and immunofluorescent findings did not correlate with the severity of proteinuria. Thus, proteinuria alone may not accurately reflect the degree of glomerular and/or podocyte damage.

sFlt UPREGULATES SYNAPTOPODIN EXPRESSION IN PODOCYTES

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Novel antiangiogenic factors have been recently implicated in the pathogenesis of preeclampsia. One such factor, the soluble fms-like tyrosine kinase (sFlt), an antagonist of VEGF, is found to be upregulated in preeclampsia. Since proteinuria is a hallmark of preeclampsia and that podocyte specific deletion of VEGF results in the endotheliosis, we believe that the podocyte is affected in preeclampsia, causing dysregulation of its complex actin cytoskeleton. We studied the effect of sFlt treatment on the cultured murine podocyte and the expression of synaptopodin, an actin-associated protein. Podocytes were treated with 0, 10, 20, 30, 90 ng/mL of sFlt-Fc chimera (R&D Systems) and analyzed by both immunofluorescence (IF) and western blotting (WB). After 2.5 hours of treatment, synaptopodin expression increased qualitatively on IF and upregulated by 2-fold in WB. There was, however, no further increase of synaptopodin with escalating doses. These results suggest that sFlt affects the integrity of the actin cytoskeleton of the podocyte, manifested by increased levels of synaptopodin. Since synaptopodin induces stress fiber formation via RhoA signaling, we are conducting additional studies of sFlt on the synaptopodin downstream pathway to better elucidate the role of sFlt on podocyte damage in preeclampsia.

ANTI CD 20 ANTIBODY IN THE TREATMENT OF MEMBRANOUS NEPHROPATHY– A THREE CASE SERIES.

Sarat Kuppachi, Naqi Idris, Lin Lwin and Jinil Yoo.

Rituximab (monoclonal antibody to B cell surface antigen CD20) has been reported to promote sustained remission for idiopathic membranous nephropathy in a 1-year prospective trial. We have used rituximab to treat three patients with biopsy proven membranous nephropathy (MN). Ptient (Pt) 1 had MN associated with thrombotic thrombocytopenic purpura (TTP), Pt 2 had autoimmune thyroiditis and idiopathic MN and the 3rd, lupus nephritis – mixed class IV and V.

Each patient was treated with IV rituximab at 375 mg/m², given as weekly infusions for a maximum of 4 weeks. Both patients 1 and 2 developed remission of disease after four doses with no adverse effects during therapy. Pt 3 received two doses as an outpatient but because of worsening of NS required admission to hospital. The 3 rd dose was given while being admitted to hospital but she developed ARDS leading to a pulmonary renal syndrome. In this series Pts1 and 2 with pure MN had remission of NS while Pt 3 with a combined pathology of diffuse lupus nephritis and MN showed no response to therapy. We believe rituximab is to be viewed as a disease remitting agent for pure MN, but the response rates to MN in combination with other nephritis may not be as promising.

MEMBRANOUS NEPHROPATHY ASSOCIATED WITH THROMBOTIC THROMBOCYTOPENIC PURPURA.

Sarat Kuppachi, Naqi Idris, Alka Walter and Jinil Yoo.

A 40 year old African American male was brought to the emergency room with complaints of confusion and fever. He was noted to have a purpuric rash, thrombocytopenia (platelet count 7,200/ml), schiztocytes on peripheral smear and renal failure (serum creatinine 1.7mg/dl). He was diagnosed to have thrombotic thrombocytopenic (TTP) and was started on high dose IV steroids and plasmapheresis. Initial antinuclear antibody screen was positive, C3 and CH50 levels were normal, C4 was low (10%), antismooth muscle and rheumatoid factor antibodies were negative. He improved symptomatically and serum creatinine normalized to 1.3 mg/dl in a week hoever while receiving daily plasmapheresis and steroids he was also discovered to have pedal edema, a serum albumin of 3.2 gm/dl and proteinuria measuring 10.24 gm/24 hr. A kidney biopsy performed to evaluate the proteinuria revealed chronic membranous glomerulopathy (MGN), with variable mesangial expansion, organized obliterative arteriopathy consistent with thrombotic microangiopathy. As his platelet count remained refractory to plasmapheresis and steroids he received one dose of vincristine to which no response was observed. He subsequently was started on rituximab (monoclonal antibody to anti CD 20) given as weekly infusions. The platelet count normalized after two doses of rituximab. Three days following the second dose of rituximab, proteinuria decreased to 3.73 gm/24 hr and 2 weeks later was 1.67 gm/24 hr. Repeat ANA screen after discharge was negative and he has remained asymptomatic for more than three years to date.

Recent studies indicate that 70-90 % of patients with acute TTP have an inhibitory antibody that causes a deficiency of a plasma metalloprotease which normally cleaves an unusually large Von Willibrand factor. It is also well known hat MGN is a type of “autoimmune nephritis”. The association between TTP and MGN has, to the best of our knowledge, been reported only once previously. We believe that the same process that led to the plasma metalloprotease deficiency led to the immune complex deposition in the kidney. Rituximab has been used with promising results in the treatment of idiopathic membranous glomerulopathy. This remission of proteinuria with rituximab leads us to believe that it can be considered as a mode of therapy even in secondary forms of MGN.

ANTI-MPO ANTIBODY SMALL VESSEL VASCULITIS PRESENTING AS PROSTATITIS AND NEPHRITIS

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Microscopic polyangiitis is a necrotizing angiitis involving capillaries, venules, and arterioles. The vascular beds of various organs may be involved causing varying presentations. To our knowledge, this is the first case of anti-myeloperoxidase (anti-MPO) antibody small vessel vasculitide causing prostatic vasculitis.

79 y/o non-smoker American male presented with symptoms of fevers, malaise, weight loss, and cough. U/A revealed hematuria. Blood tests were remarkable for an elevated PSA and a serum creatinine of 3.1 mg/dl (baseline 1.2 mg/dl). CT scan of the thorax revealed a 4.7 cm left lower lobe mass. Metastatic prostate cancer was suspected. Therefore, prostatic biopsy was performed. The biopsy revealed fibrinoid degeneration with vasculitic changes involving the arterioles.

When evaluated by nephrology, his serum creatinine was 9.9 mg/dl. A renal biopsy was performed which revealed focal segmental necrotizing glomerulopathy with microscopic vasculitis. All the serologies were normal with the exception of a low C4, and a positive P-ANCA associated with anti-MPO. Pt was started on intermittent hemodialysis, steroids and oral cytoxan.

Vasculitic involvement of the prostate is an uncommon manifestation of microscopic polyangiitis. This bedazzling entity is challenging to diagnose and thus makes it difficult to treat in a timely manner.

ATYPICAL PRESENTATION OF THROMBOTIC MICROANGIOPATHY

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This report details a family with thrombotic microangiopathy (TMA) spanning three generations. The index case A, age 21, was initially referred for evaluation of proteinuria. Preliminary investigations revealed hypertension, normal renal function, normal renal size by ultrasound and sub-nephrotic range proteinuria. A percutaneous renal biopsy was performed revealing a pattern consistent with chronic TMA.

A's mother has spastic paraparesis and underwent renal biopsy 20 years ago; she was initially given a diagnosis of adult-onset nephronophthisis. She progressed to end-stage kidney disease (ESKD) and required 7 months of haemodialysis before receiving a cadaveric renal transplant. A's maternal aunt had spastic paraparesis, seizure disorder and also carried a diagnosis of nephronophthisis. She too progressed to ESKD and received a renal transplant, but passed away before further evaluation. A second maternal aunt attends the Nephrology clinic with hypertension, renal impairment and sub-nephrotic rage proteinuria.

A's two brothers were evaluated and found to have renal impairment, sub-nephrotic range proteinuria and hypertension. A renal biopsy revealed histology consistent with TMA in one of the brothers.

Finally, A's maternal grandmother and grand-aunt were known to have kidney disease. It is unclear from records whether they were given a formal diagnosis.

Thrombophilia screens and von Willebrand Factor protease cleaving activity have been normal in all patients tested. In addition Factor H and Factor I levels in A, as well as genetic analysis for Factor H mutations, were all normal.

Given the strong pedigree of kidney disease and the presence of TMA on two recent biopsies, it is likely that this family all suffer from the same disease process. Further genetic testing is in progress but has failed to identify a specific diagnosis as yet. This series highlights the myriad of clinical conditions that can lead to a pattern of TMA.

RESOLUTION OF STEROID-DEPENDENCY BY A DAIRY/HYPOALLERGENIC DIET IN CHILDREN WITH NEPHOTIC SYNDROME.

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Most children with nephrotic syndrome (NS) respond to glucocorticoids (remission). However, relapses are very common. Many receive glucocorticoids for years to sustain remission. Cyclophosphamide may help these "steroid-dependent" children, but it has potential side effects including serious infections, sterility and malignancy. Thirty years ago, Sandberg et al had illustrated a substantial reduction in proteinuria by eliminating cow's milk from the diet of several patients. Few subsequent studies demonstrated remission of NS by eliminating dairy products or other allergenic foods. We report our experience in four children with steroid-dependent nephrotic syndrome whom we managed by cow's milk free/oligoantigenic diet rather than prescribing cyclophosphamide. They were between 4-10 years old when the diets were initiated. Glucocorticoids were tapered similarly as had been done after previous remissions. Case 1 received the diet for one year. He has remained in remission for nine years. Case 2 received it for 2 years. He remained in remission for 27 months. Case 3 was on a cow's milk free diet for 7 months before she relapsed. Case 4 has been on the diet for 13 months. She remains in remission. We conclude that restricting diet, rather than prescribing cyclophosphamide, may be extremely helpful in managing children with steroid-dependent nephrotic syndrome. A controlled study is in progress.

AORTIC THROMBOSIS IN AN ADULT PATIENT WITH MINIMAL CHANGE NEPHROTIC SYNDROME AND HODGKIN'S LYMPHOMA: A RARE ASSOCIATION AND COMPLICATION.

E. Sarac, H. Zhang, H. Negrete, J. Spalding, D. Gemmel.

A 48 year old Caucasian male presented with complaints of generalized fatigue and swelling of legs for four days in June 2006. His medical history included Hodgkin's lymphoma diagnosed and treated with subsequent remission in 2002 and heavy tobacco use. The physical examination revealed edematous and cyanotic legs with no palpable pulses. His hemoglobin was 19g/dL, along with BUN of 21 mg/dL and serum creatinine of 1.5 mg/dL. Serum albumin was 1.5g/dL with urine protein on urinalysis greater than 300 mg/dl.

CT angiogram of chest and abdomen revealed a 1.5cm in diameter of thrombus in the aortic arch extending into the left common carotid artery. In addition, another thrombus of 1.2-1.3cm in diameter was in the mid descending aorta and there were scattered thrombi of various sizes more distally with the aorta. An emergent operation for thrombectomy was performed through femoral and brachial artery approaches and intravenous anticoagulation therapy was initiated. Postoperatively, patient developed acute renal failure. A renal biopsy performed showed minimal change disease along with recovering acute tubular necrosis. Temporary hemodialysis along with daily oral steroid therapy was initiated with prednisone. After eight weeks of steroid therapy the renal failure and nephrotic proteinuria resolved.

Minimal change nephrotic syndrome (MCNS) is infrequently associated with Hodgkin's lymphoma. The complication of aortic artery thrombosis in patient with MCNS proceeded after Hodgkin's disease is a very rare presentation with only one case reported in the literature. According to our knowledge large thrombosis in the ascending and descending aortic artery presenting simultaneously in a patient with MCNS and Hodgkin's lymphoma has not been reported. We believe this is the first report of a 48 year-old male with MCNS presenting with ascending and descending aortic artery thrombosis.

NEPHROTIC SYNDROME ASSOCIATED WITH CHRONIC LYMPHOCYTIC LEUKEMIA.

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We present a case of nephrotic syndrome from minimal change disease (MCD) in a patient with chronic lymphocytic leukemia (CLL). Nephrotic syndrome is rarely associated with CLL and the predominant underlying pathology is Membranoproliferative glomerulonephritis (MPGN). We hypothesize that nephrotic syndrome from MCD in CLL is a paraneoplastic phenomenon.

A 43 years old male presented with chief complaint of swelling of lower extremities of 6 weeks duration. He was diagnosed with CLL 10 years ago. He underwent chemotherapy 7 years after diagnosis and was in chronic remission at the time of presentation. Physical examination showed a weight gain of 20 pounds and blood pressure of 140/70. He had splenomegaly, lymphadenopathy, 3 + lower extremity pitting edema with no jugular venous distension and regular heart sounds. Labs showed a WBC of 4.9, platelets 220 with 26 % lymphocytes, Na 137 mEq/L, Bun 13 mg/dL, creatinine 1.3 mg/dL, total protein 4.4 g/dL, albumin 2.3 g/dL, cholesterol 423 mg/dL, LDL 329 mg/dL and BNP 18. Urinalysis showed proteinuria with no RBC`s and casts. Urine protein/creatinine ratio was 11. P ANCA, C ANCA and ANA were normal. Anti dsDNA, RPR, HIV ELISA, Hepatitis C antibodies, HepBsAg and Anti HBsAg antibodies were non reactive. Serum protein electrophoresis did not show an M spike. He was started on Lisinopril. Kidney biopsy was consistent with MCD. He was started on Prednisone with normalization of protein creatinine ratio.

The frequency of nephrotic syndrome in CLL is less than 1 %. At least 46 cases of nephrotic syndrome in patients with CLL have been reported. MPGN is the predominant renal pathology. So far only 5 cases of MCD with CLL have been reported. The exact pathogenetic mechanism is not clearly known. CLL is a disorder of B cells. It is now recognized that there are T cell abnormalities in CLL including increase in the number of suppressor T cells. MCD may be related to excessive suppressor T cell activity. In addition T cell disorder can result in increase in soluble factors that alter glomerular permeability. It has also been postulated that patient with low expression of CD 5 positive cells develop MCD instead of MPGN.

ACUTE RENAL FAILURE SECONDARY TO SEVERE TYPE I CRYOGLOBULINEMIA FOLLOWING RITUXIMAB THERAPY FOR WALDENSTROM'S MACROGLOBULINEMIA

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Waldenstrom's Macroglobulinemia is a rare lymphoproliferative disorder characterized by the presence of a monoclonal IgM paraproteinemia. Cryoglobulinemia is a common sequela of Waldenstrom's macroglobulinemia, present in 8% - 18% of the cases. In a previous report, cryoglobulinemia has been described after the treatment with Rituximab, but no adverse effects were noted. We present a case of Waldenstrom's macroglobulinemia in which Rituximab induced cryoglobulinemia resulted in acute renal failure (ARF). An 80 year male presented to his physician with recurrent episodes of epistaxis. Evaluation showed a monoclonal protein spike of 1.9g/dL, identified as IgM kappa on immunofixation. Bone marrow biopsy revealed 60% involvement by kappa light chain restricted lymphoplasmacytic lymphoma. Skeletal survey was negative for lytic lesions. Diagnosis of Waldenstrom's macroglobulinemia was made and treatment was started with Rituximab at 375 mg/m² weekly. One week after the 3rd dose, patient developed dyspnea. On admission to the hospital, he was found to have ARF with a creatinine of 2.7 mg/dL (baseline = 1.3 mg/ dL). Urine microscopy was normal and 24 hour urine showed 475 mg of protein. Kidney biopsy showed mesangial hypercellularity along with endocapillary proliferation. The glomerular capillaries had intraluminal PAS positive deposits consistent with cryoglobulins. A type I cryoglobulin consisting of IgM kappa was detected at a level of 63% in the serum. Plasmapheresis was initiated and after 4 sessions, his creatinine declined from 3.1 mg/dL to 2.2 mg/dL and repeat cryoglobulin level was found to be 50%. He received another 4 sessions of plasmapheresis and his creatinine improved further to 1.7 mg/dL and cryoglobulin level declined to 11%. Treatment with Chlorambucil was initiated at the completion of plasmapheresis. This case illustrates that Rituximab induced cryoglobulinemia is not always benign and can result in ARF. Therefore, monitoring of cryoglobulins is advisable in cases of Waldenstrom's macroglobulinemia, both before and after Rituximab therapy.

COMBINATION USE OF ACE/ARB IN THE INITIAL TREATMENT OF LOIN PAIN HEMATURIA SYNDROME. Kate Tretyakov, Adam Dratch, Richard Snyder, Easton Hospital/Drexel University College of Medicine, Easton, PA.

Loin-pain hematuria syndrome is a poorly understood condition usually consisting of the triad of flank pain, hematuria, and low grade fever. The pathogenesis remains obscure, with theories ranging from increased intraglomerular pressure to increased sympathetic tone, and/or increased neuronal sensitivity. As such, no standard treatment or initial approach to a patient with LPHS has ever been promoted. We present the case of a patient diagnosed with loin-pain hematuria syndrome (LPHS) who was initially treated with an ACE/ARB combination with some relief from her pain.

A 35-year-old female presented with the triad of flank pain, hematuria, and low grade fever. Recurrent CT scans failed to identify a stone or filling defect. A urologic examination and CT angiogram were nondiagnostic. Creatinine of 0.9 mg/dl and no protein was seen on a p/c ratio. There was no significant proteinuria, and a renal biopsy demonstrated thin basement membrane disease. We postulated a diagnosis of LPHS. The patient was initially started on valsartan 80 mg, and a week later lisinopril 5 mg was added. The patient still complained of some mild flank discomfort, but noted a significant decrease in her pain level compared to when she was not on those medications. The patient's pain gradually increased and pain medication was added. She was subsequently referred to a tertiary referral center and surgery was performed, which dramatically helped her symptoms. We feel that combination ACE/ARB therapy in conjunction with pain management may be an effective initial therapy in this condition. Further studies are needed in this area.

EFFECT OF BLOCKING THE RENIN ANGIOTENSIN ALDOSTERONE SYTEM (RAAS) ON REFRACTORY FOCAL SEGMENTAL GLOMERULOSCLEROSIS (FSGS) TO LOWER BLOOD PRESSURE AND DECREASE PROTEINURIA TO PRESERVE GLOMERULAR FILTRATION RATE (GFR) AND SLOW PROGRESSION TO END STAGE RENAL DISEASE (ESRD)

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FSGS leads to rapidly progressive scarring or sclerosing of capillaries, deterioration of kidney function and ESRD, dialysis/transplantation. FSGS causes proteinuria (P) from asymptomatic microalbuminuria to large symptomatic nephrotic syndrome, >3,500mg/24h and hypertension.

We treated 8 patients 3-5 years with kidney biopsy proven FSGS. Serial studies included P, BP, electrolytes, serum creatinine and GFR in response to combination therapy interfering with the RAAS. Medications were in 4 categories: I.Angiotensin-Converting Enzyme Inhibitors (ACE I), II.Angiotensin Receptor Blockers (ARB), and III.Aldosterone Receptor Antagonist (ARA) or Selective ARA (SARA) plus IV.immunosuppressives, corticosteroids and mycophenolate. Poor response to corticosteroids defined refractory. Mycophenalate was used as a last resort.

As medications were added, a decrease in P occurred in 8/8 patients. Treatment with 3 drugs blocking the RAAS caused progressive reduction of BP and P preventing rapid deterioration of GFR in all 8 patients while adhering to the therapeutic regimen. In 6/8 long term compliant patients, P and BP were reduced progressively. 2/8 patients became delinquent and noncompliant leading to rapid reduction of GFR and subsequent hemodialysis within 6-9 months.

FSGS prognosis correlates with BP & P reduction preventing ESRD. Anti-RAAS treatment effectively reduced P and BP in 8/8 patients while compliant, slowing down the loss of GFR. 2 Anti-RAAS noncompliant patients had rapid deterioration of kidney function requiring hemodialysis. Patients with FSGS should be treated early and continuously with combinations of Anti-RAAS medications. Frequent testing of potassium and creatinine are required. Future larger trials are in design.

BLEEDING COMPLICATIONS OF RENAL BIOPSY

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The introduction of automated biopsy devices and the localization of the kidney by ultrasound were aimed at optimizing efficacy and safety of the percutaneous renal biopsy procedure. We evaluated the safety of Tru Cut biopsy needle 14G (1974-1990) and core tissue biopsy needle 16G with automated biopsy device 16G (1990-2005). Fluoroscopy was used to localize the kidney until 1990 and direct ultrasound guidance after. The occurrence of macroscopic hematuria in patients biopsied with Tru Cut needle (545) was 6,7%, 13% of the biopsied patient required blood transfusions. Subcapsular hematoms were not observed, possibly because ultrasound had not been introduced and computerized tomography was not a routine procedure. Macroscopic hematuria was observed in 6,9% patients biopsied with core tissue biopsy needle (total number 1192 patients). None of these patients required blood transfusion. Subcapsular hematomas were noted 2,3% patients, one of them with rupture in peritoneal cavity and requirement of repeated blood transfusions. Summerizing the results we can conclude that there was not significant difference between these two procedures of percutaneous renal biopsy.

LINE REVERSAL OF TUNNELED DIALYSIS CATHETERS AND ITS IMPACT ON RECIRCULATION

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The tunneled dialysis catheter (TDC) carries the highest incidence of hemodialysis vascular access at the initiation of dialysis. When inflow failure (i.e.: the inability to obtain a sufficient blood pump flow [QB]) occurs during dialysis, it is common practice to reverse the blood lines. The purpose of this study is to determine if there is a significant difference in the recirculation rate between normal and reversed lines using well functioning tunneled catheters.

Ten hemodialysis patients (male/female ratio: 3/7) with well functioning (achieving QB> 400ml/min) right internal jugular vein TDC (with tip positioned in the right atrium) were included. For each patient, recirculation rate measurements were obtained during three random dialysis sessions. In each session recirculation rate was measured at blood pump flow rate of 300ml/min and 400ml/min in both normal and reversed position respectively. Each subject had four readings per dialysis session (i.e. a total of 120 readings) using the ultrasound dilution technique (Transonics, Ithaca, NY).

Reversal of blood lines in TDC significantly increased recirculation rates. The recirculation rate increased from 1.2 $\pm$ 3 to 21.5$\pm$12% ($p< 0.0001$) at QB of 300ml/min and from 1.7$\pm$4 to 25.2$\pm$13% at QB of 400ml/min ($p< 0.0001$) between normal and reversed lines, respectively. In addition, there was no significant change in the recirculation rate between QB of 300ml/min and 400 ml/min within the same blood line position.

In conclusion, the use of TDC in reversed lines' position can lead to significantly higher recirculation rates and possibly resulting in less adequate hemodialysis. Exchanging the TDC may be the best approach in TDC with inflow problems rather then reversing the lines. However, further evaluation of the impact of this significant rise in the recirculation rate on the adequacy of dialysis should be conducted to support this recommendation.

SUCCESSFUL PREGNACY OUTCOME IN A NONCOMPLIANT PATEINT ON CHRONIC HEMODIALYSIS (HD)

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Overall frequency of pregnancy remains uncommon in dialysis patients. The outcome of pregnancies in women who get pregnant while being on dialysis remains poor. We report a case of successful pregnancy in terms of both maternal and fetal outcomes in a noncompliant patient on chronic HD. Our patient is a 37 year old African American female (P3063) with history of hypertension, on chronic HD for about 2 years secondary to glomerulonephritis, obesity, cocaine use in past. While being on HD she was diagnosed to be pregnant based on an incidental finding of elevated serum beta hCG levels drawn in emergency room as patient was being evaluated for cough and needed an X-ray. Patient was explained about the associated maternal and fetal risks and possibilities of the outcomes. At her first antenatal visit the gestation was estimated to be 16 weeks by ultrasonography.

Patient's medications were reviewed and a multidisciplinary team was made comprising of the nephrologists, dietician, social worker and dialysis nurse. The care was coordinated between the nephrologists and obstetrician. More intensive HD was planned as per current recommendations but patient couldn't adhere to the plan and continued to receive 12-14 hours of HD /week in place of proposed 20 hours /week. Careful and frequent dry weight adjustments were made, erythropoietin dose was adjusted and IV iron was continued. Patient continued to smoke during pregnancy and missed several follow-ups with obstetrics. At 34 weeks of gestation patient delivered a 1965 gram baby with Apgar score 9/9, by normal vaginal delivery. Despite delayed diagnosis, inability to adhere with more intensive dialysis plan patient had a successful outcome.

The current guidelines for dialysis in pregnancy are all based on anecdotal case reports, single center retrospective reviews and survey reports as the overall frequency of pregnancy in this population remains low and with each report we are getting more information on this unique group on dialysis.

INFECTION PATTERN IN HIV INFECTED HEMODIALYSIS PATIENTS

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HIV-Infected patients are more susceptible to viral and opportunistic infection. We conducted a retrospective study to see pattern of infection in HIV positive hemodialysis patients.

Inpatient charts of 44 HIV positive hemodialysis patients were reviewed for evidence of infection over a period of 3 years. Appropriate cultures were performed with the signs and symptoms of infections such as: fever, chills, drainage of pus, cough, or signs of sepsis including hypotension.

Thirty out of 44 HIV positive HD patients met the criteria of suspected infection. These 30 patients had 98 cultures from blood, urine, wound, sputum, and CSF during the duration of study. Cultures were positive in following order: 26 out of 62 blood cultures, 2 out of 10 urine cultures, 5 out of 8 wound culture, 5 out of 16 sputum cultures, and 2 out of 2 CSF cultures. Out of all positive cultures, 65% were blood borne, the majority or 19 (73%) patients had gram positive organisms, 6 (23%) had gram negative bacteremia and 1 (4%) had Candida septicemia. Only 4 (13%) pts had opportunistic infections, i.e. 1 had Candida esophagitis, 1 had toxoplasmosis in brain, and 2 had cryptococcal meningitis.

We found out that most common infection in HIV positive dialysis patients is due to gram positive organisms.

EFFECTIVE HEMOGLOBIN (HB) CONTROL WITH EPOGEN (EPOETIN ALFA) IN THE REAL-WORLD CLINICAL SETTING

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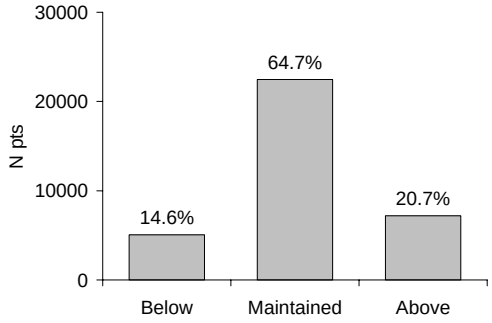
We assessed Hb outcomes in hemodialysis (HD) patients in the real-world clinical setting, which allows for flexible Epoetin alfa dosages in response to Hb changes associated with intercurrent events and comorbidities. The study was based on an internal database that contained all Hb measurements for HD patients treated in the US in 2005. Patients were included in the study if they had at least 12 weeks of HD followed by a 4-week baseline period during which all Hb values were maintained within 10.5 and 13 g/dL and were to vary no more than 1 g/dL. We compared average Hb level over the 4 weeks of the baseline period, and over the 8 weeks of the evaluation period (starting 28 weeks after the end of baseline period).

In 34,718 patients, 64.7% had Hb values during the evaluation period that were ±1 g/dL of the baseline level (Figure). Our results show that Epoetin alfa is able to maintain effective control of anemia in a real-world HD population with stable baseline Hb. This result, using actual US practice patterns and Epoetin alfa dosing, was very similar to recent clinical trials, where approximately 68% of HD patients on CERA (peg-EPO) therapy maintained Hb levels within ±1 g/dL of baseline using this same methodology in a population selected by strict inclusion and exclusion criteria.



HEMATIDE™, A SYNTHETIC PEPTIDE-BASED ERYTHROPOIESIS STIMULATING AGENT, MAINTAINS HEMOGLOBIN IN HEMODIALYSIS PATIENTS PREVIOUSLY TREATED WITH EPOETIN ALFA (EPO)

A Besarab[1], S Zeig[2], R Geronemus[3], P Pergola[4], F Whittier[5], R Zabaneh[6], B Schiller[7], M Kaplan[8], N Levin[9], S Wright[10], S Swan[11], R Wintz[12], D Wombolt[13], R Leong[14], W Lang[14], M Franco[14], and AM Duliege[14]. [1]Detroit, MI; [2]Pembroke Pines, FL; [3]Lauderdale Lakes, FL; [4]San Antonio, TX; [5]Canton, OH; [6]Shreveport, LA; [7]Mountain View, CA; [8]Nashville, TN; [9]New York, NY; [10]Pine Bluff, AR; [11]Minneapolis, MN; [12]Los Angeles, CA; [13]Norfolk, VA; and [14]Palo Alto, CA, US.

Hematide, a novel synthetic PEGylated peptide that binds to and activates the erythropoietin receptor, is being developed for treatment of anemia in CKD patients. This abstract reports on the findings of a Phase 2, open-label, multi-dose study conducted to assess safety and pharmacodynamics of Hematide in hemodialysis patients with stable baseline Hb 10 to 12.5 g/dL previously on EPO.

Patients discontinue EPO to receive up to 6 doses of IV Hematide once every 4 weeks (Q4W). Dose adjustments based on Hb levels are allowed with the goal of avoiding Hb >13 or <10.5 g/dL. Preliminary data for the first 120 patients from 8 cohorts have been analyzed.

The mean baseline Hb was 11.4 g/dL. Apart from variations in TSAT and ferritin, baseline characteristics were balanced across cohorts.

Initial Hematide doses of 0.050 and 0.066 mg/kg Q4W per 100 U/kg/wk EPO maintained mean Hb values within 1 g/dL of baseline when initiated 1 week after last EPO dose (i.e., washout); without washout, 24% of patients required dose delay. Initial tiered, weight-based Hematide doses of 0.05 to 0.15 mg/kg, also based on previous EPO requirements, maintained mean Hb values within 1 g/dL of baseline, with or without washout. One patient had a drug-related rash. Over a period of 16 months, 47 SAEs were reported: 46 were non-drug related, and one Grade 2 infusion reaction responding to outpatient intervention was considered possibly/probably related to study drug.

Preliminary data suggest that Hematide is well-tolerated, is pharmacodynamically active, and may be dosed Q4W. Hematide will be evaluated in Phase 3 clinical trials in both hemodialysis and predialysis CKD patients.

UREMIC PRURITUS PATIENTS: A NATIONAL SURVEY OF SLEEP AND MOOD DISRUPTIONS

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Previous data have suggested that there is a relation between uremic pruritus (UP) and sleep disruption, mood, and mortality. To understand the prevalence of sleep and mood disruptions, a Web-based survey was conducted in 101 UP patients who had been treated with hemodialysis 2 to 4 times a week for $\geq$6 months. Patients were self-classified, using a multidimensional categorical scale, as having mild (n=5), moderate (n=69), or severe (n=27) UP. The mean age was 36 $\pm$ 9 years, 51% were male, and mean time on hemodialysis was 14 $\pm$ 9 months. There was a strong correlation between the severity of UP and the effect on patient mood. Itching also had an impact on sleep. Forty percent of patients with mild UP, 89% of patients with moderate UP, and 85% of patients with severe UP reported having at least 1 night of sleep a week disrupted . Moreover, 38% of moderate and 52% of severe UP patients reported having 3 or more nights of sleep a week disrupted by pruritus. Sixty-three percent of patients stated that their dialysis physicians had done nothing to treat their pruritus. This survey indicates that sleep and mood disruptions in patients with all levels of severity of UP are common and correlate with disease severity.

AMBULATORY BLOOD PRESSURE (BP) MONITORING IN THE DIALYSIS POPULATION: IS IT ESSENTIAL?

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Hypertension is endemic in the dialysis population. Nephrologists rely on routine blood pressure (RBP) measurements of pre-dialysis blood pressure (Pre-BP) and post-dialsysis blood pressure (Post-BP) to assess hypertension. Current K-DOQI guidelines recommend target Pre-BP and Post-BP of 140/90 and 130/80, respectively. The purpose of this study was to assess the relationship of RBP measurements to ambulatory blood pressure (ABP) measurements and to determine the burden of uncontrolled hypertension in our hemodialysis population with ABP measurements.

RBP measurements were made by trained dialysis staff with patients after sitting 5 minutes before and after dialysis. Six RBP measurements were averaged, pre and post dialysis. ABP were measured between the 5^{th} and 6^{th} RBP measurements over the 44-hour interdialytic period with Spacelab ABP monitors. Mean ± SD BP (mmHg) using both techniques were compared using the paired t-test.

With n=35, the mean ABP was 135.5±22.8/80.3±15.1. Mean Pre-BP averaged 162.6±22.4/ 88.2± 13.9 ($p < .0001$), while Post-BP averaged 148.8±23.8/80.6±13.4 ($p < .0001$ for systolic pressure). The percentage of subjects with a systolic blood pressure greater than the goal was 40% for ABP, 84.4% for Pre-RBP, and 75.8% for Post-RBP. The percentage of subjects with a diastolic greater than the goal was 22.9% for ABP, 40.6% for Pre-RBP, and 39.4% for Post-RBP.

ABP demonstrates BP significantly less than either the pre/post dialysis blood pressures. Routine pre/post blood pressures therefore may overestimate the true burden of hypertension in this patient population. When blood pressures are measured using an average of ABP, a significantly lower percentage of participants were above blood pressure targets.

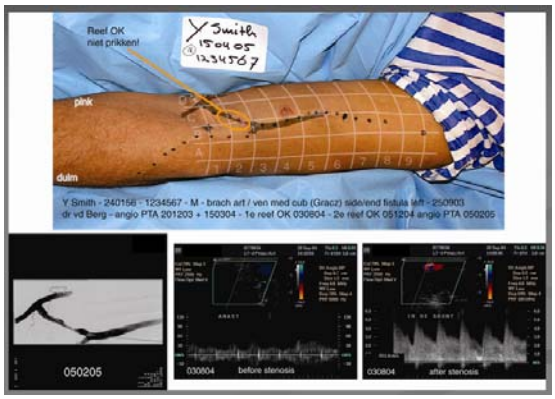
CUSTOM MADE RASTERMETHOD FOR FISTULA AND GRAFT

Cees Blokker, EDTNA / LVDT / VAS

Unfamiliarity with fistula and graft characteristics can lead to failed punctures, haematoma and sometimes access occlusion. The Custom-made Raster Method provides detailed shunt visualisation and angiographic images together by using photo editing software. Access veins of an individual shunt and an adapted raster are projected on a digital picture of the arm.

During angiography the shunt arm is fixated and a digital picture is taken from a fixed vertical angle and distance. Reference points are marked on the shunt arm, which serves as a fixation to draw a raster with coordination points. In this way a picture is created like a roadmap with veins. There is complete integration of digitally and radiology images by using software programs (Adobe Photoshop® + Illustrator® en Agfa Web 1000®) under Windows XP®. All Illustrations are made fit 1:1 by scaling up or down without distortion. Editing with Photoshop® gives a precise projection of shunt veins on the real coloured background of the digital photograph. In this projection the grey angiography background is made completely transparent. The system can contain more detailed information in combination with original angiography pictures and echo (duplex) images of depth and diameter.

This visualisation method is a useful tool for multi disciplinary access meetings with intervention Radiologists, Access Surgeons and Nephrologists. Access malfunction, aneurysms, stenosis and even stents can be projected at the exact location. The system leads to clear and concrete puncture advise. Transfer of access information and communication to intervention specialists and other dialysis centers is facilitated.



LOOKING THROUGH THE FISHBOWL: LESSONS LEARNED FROM THE CAHPS ICH QUALITY IMPROVEMENT PROJECT

Dawn Wilson, DaVita Covington Dialysis, Covington, Virginia, USA

DaVita Covington Dialysis was one of seven dialysis facilities across the U. S. selected in a research project sponsored by CMS and conducted by the American Institutes for Research(AIR). The Consumer Assessment of Health Care Plans Services In-Center Hemodialysis(CAHPS-ICH) Quality Improvement Project was initiated in August of 2005 and completed by September of 2006. A sample of patients from each unit was surveyed comprehensively by phone on a variety of dialysis-related services ranging from cleanliness of the facility to staff professionalism. Facility staff then selected a problem identified in the survey for improvement The Agency for Healthcare Research and Quality, AIR and renal networks provided and support.

DaVita Covington Dialysis is a small facility of approximately 40 pts. located in rural Virginia. The population is mostly white, >35 years of age, reporting health as good to poor. Covington's Improvement Focus Area was to "improve patients' perceptions of staff availability and responsiveness to concerns" based on 49% response in 2005 that patients were "Sometimes or Never" satisfied with how staff handled problems occurring during dialysis. Through staff training, including the MD, the unit assumed a more "customer-friendly" approach to services. During this time period DaVita acquired the Covington facility, a corporate environmental change that resulted in significant, and serendipitous, changes in the unit. Staff committed to various team-building tactics such as daily "homeroom" meetings and positive, patient-centered activities. The unit also began utilizing facility volunteers to provide support and act as liaisons between staff and patients. Patient representatives are also available to articulate concerns for patients who are uncomfortable in expressing complaints directly.

The follow-up results compiled by AIR in 2006 showed a significant decrease in problems, and improvement in measures such as timeliness and effectiveness in addressing problems. At the CAHPS Summit Meeting in September of 2006, the DaVita Covington facility stated a commitment to share their findings with others in the renal community to hopefully increase patients' satisfaction with their dialysis services.

THE ASSOCATION BETWEEN GLYCOSYLATED HEMOGLOBIN (HgbA1c) AND THREE-YEAR MORTALITY RISK IN PATIENTS ON MAINTENANCE HEMODIALYSIS.

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We reported that HgbA1c was associated with 1-year death risk at high and low extreme values (Williams et al, KI, 2006). This report extends the follow-up of these patients over 3 years.

Hemodialysis (HD) patients in the database of a large dialysis organization with a diagnosis of diabetes, HgbA1c results from Oct. 1 to Dec. 31, 2002, and survival into Jan. 1, 2003 formed the study cohort. They were followed from Jan. 1, 2003 to Dec. 31, 2005. Cox models were used to determine unadjusted, case-mix adjusted (age, gender, race, body surface area, and vintage) and fully adjusted (case mix plus vascular access type, eKt/V, albumin, hemoglobin, phosphorus, and WBC) mortality risk profiles.

There were 24,875 patients with mean age 63.7 $\pm$ 12 years, 52% female, 53% white and 36% black, 94% type 2 diabetic, with mean HgbA1c 6.77%, eKt/V 1.41, Hgb 11.7 g/dL, and albumin 3.82 g/L, in the cohort. Mean HgbA1c > 11% is associated with a ~23% higher risk of death over 3 years ($p < 0.05$), after adjusting for case-mix, access type, and selected laboratory variables. However, the risk profile is flat over the distribution of HgbA1c < 11%.

Findings support keeping HgbA1c < 11%. However, more research is needed to further refine the utility of HgbA1c tests and define outcome-based HgbA1c targets in HD patients.

RETROSPECTIVE EVALUATION OF VECTRA GRAFTS VS. PTFE GRAFTS FOR HEMODIALYSIS PATIENTS.

Janice Weatherspoon, Ivan Maya, Carlton Young, Michael Allon. University of Alabama at Birmingham. Divisions of Nephrology and Transplant Surgery. Birmingham. AL

Conventional PTFE dialysis grafts cannot be cannulated for 2-3 weeks following their creation. In contrast, the Vectra graft, made of a self-sealing polyurethane material, can be cannulated within 24 hours of implantation, representing a potential advantage in patients with limited catheter options. Since FDA approval of the Vectra graft in December 2000, little has been published on the relative outcomes of Vectra and PTFE grafts.

Using a prospective, computerized vascular access database we identified 31 patients with a Vectra graft placed between 7/1/01 and 6/30/06, and compared them to 56 date-matched controls with a standard PTFE graft. The Vectra and PTFE groups were comparable in terms of age (55 vs 58), sex (39 vs 35% females), race (95 vs 98% blacks), diabetes (48 vs 42%), HTN (96 vs 90%), CAD (23 vs 29%), PVD (13 vs 6%), and proportion of thigh grafts (55 vs 55%).

The median thrombosis-free graft survival (from creation to first thrombosis or failure) was similar for Vectra and PTFE grafts (median, 189 vs 216 days; 1-year survival, 29 vs 37%, P=0.52). The cumulative graft survival (from creation to permanent failure) was also similar (median, 987 vs 1098 days; 1-year survival 60 vs 60%, P=0.93). Finally, the cumulative risk of graft infection was 37.5% for thigh Vectras, 23% for upper arm Vectras, 21% for thigh PTFE, and 5% for upper arm PTFE (P=0.015 for the trend).

In conclusion, the likelihood of thrombosis and failure is similar for Vectra and PTFE grafts. However, Vectra grafts have a higher risk of infection, particularly when they are placed in the thigh. Implantation of a Vectra graft represents a tradeoff between earlier cannulation and higher risk of infection.

PROMOTING SELF-CARE IN HEMODIALYSIS

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Positive adjustment to hemodialysis is a key determinant in the quality of life and longevity for individuals with CKD (Chronic Kidney Disease). Social workers assist with the adjustment to illness and improved quality of life by providing education, supportive counseling, advocacy, and facilitating patient to staff, and patient to patient interactions. Promoting self-care in addition to these services empowers patients to gain control and independence.

In collaboration with the multidisciplinary team, social workers surveyed patients in the unit to assess their interest and willingness to engage in a self-care program. All interested candidates received literature regarding the latest education and information for self-care, cannulation, and the importance of vascular access, a glossary of treatment terms and medications, and various dialysis machine specifics. Self-care began with patients obtaining their own temperatures and weights, cleaning their access site, with progression to self-cannulation; under the supervision of clinical staff. This process was expected to preserve their access, increase patients' sense of control and decrease rates of hospitalization.

Creating a self-care program utilizing social workers as program developers and change agents proved effective at Greenfield Health Systems-Detroit Northwest Dialysis and Lahser Units. Social work interventions with staff and patients were successful as evidenced by an increased number of patients practicing self-care techniques and a significant number of those self-cannulating. This was achieved through positive rapports, education, peer mentoring, and individual coaching with motivational techniques.

In conclusion, the social worker's formal education and training to assess, counsel, empower, educate and advocate proved foundational to increasing patient satisfaction and participation in their medical regimen while improving quality of life.

CARNITINE EFFEVTIVENESS ON INTRADIALYTIC HYPOTENSION

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Intradialytic hypotension (IDH) in end-stage renal disease patients is a common complication of hemodialysis (HD). In some patients IDH is refractory to standard interventions including reduced ultrafiltration, sodium modeling and cold dialysate. In two small, randomized, controlled trials L-carnitine was shown to reduce IDH. The objective of our study was to confirm that L-carnitine is effective in reducing IDH.

We retrospectively reviewed the charts of 9 patients at a single dialysis center who received L-carnitine for IDH. All had IDH and L-carnitine levels $\leq$ 40 mmol/L. IDH was defined as a sudden drop in systolic blood pressure (SBP) <90mmHg, a more than 30mmHg drop mean arterial pressure (MAP), or a more than 30mmHg drop in SBP from baseline. Every blood pressure from every HD session was recorded for the 4 weeks prior to the L-carnitine order and for 24 weeks of L-carnitine administration. To account for a possibility that duration of treatment was important we divided the treatment period into three: first 20 doses, second 20 doses, and thereafter.

We found significant improvement following the initiation of L-carnitine in multiple measures of IDH. Sudden drops in SBP > 30mmHg fell 22% from the control period to the 3rd period (p=0.015). Drops in SBP from baseline fell 24% (p=0.001). SBP falling below 90 mmHg fell 55% (p=0.039). During the treatment period there was no change in ultrafiltration, dry weight, or pre-dialysis SBP. Pre-dialysis MAP and a modest increase in post-HD MAP from 88.7 to 90.7 were also found to be significant (p=0.017).

In this retrospective analysis L-carnitine use was associated with significant improvement in IDH. This improvement increased with longer duration of administration. This data further highlights the need for a large randomized placebo controlled trial to confirm the utility of L-carnitine for IHD.

DIETARY PITFALL OF CHRISTMAS EVE AND NEW YEAR'S EVE ON WEEKENDS IN PATIENTS UNDERGOING MAINTENANCE HEMODIALYSIS. Kimiko Takahashi, Emi Kihara, Seiji Kawahara, Nanako Ikari, Kazuko Arita, Katsutoshi Maeda and Hiroaki Oda, Oda medical Clinic, Hiroshima, Japan. Both Christmas Eve and New Year's Eve in 2005 were Saturdays and patients undergoing hemodialysis enjoyed their weekends eating special food and drink without dialysis therapy for two days. Increase in body weights and elevation of serum concentrations of urea nitrogen, creatitine (Cr), uric acids (UA) and phosphate (P) were predicted. The purpose of this study was to clarify the characteristics of food during these holiday seasons and the effects on the clinical features revealed by serum concentrations in hemodialysis patients. Eighty-four patients (male/female; 56/28, 61.6 years) for Christmas Eve and 74 patients (male/female; 44/30, 62.5 years) for New Year's Eve were subjected to this study. Increase in body weights and serum concentrations of urea nitrogen, Cr, UA, P, potassium (K), sodium (Na), chloride (Cl), calcium (Ca), lipid profile and albumin (Alb) were measured just before and after the weekends of Christmas and the New year. Nutrition investigation was conducted in 16 patients with much increase in body weight during these weekends. Data were analyzed using paired t-test and $p<0.05$ were considered statistically significant. Significant increase in body weight during Christmas (+2.4 v.s. +2.2 kg) and the New Year (+2.6 v.s. +2.4 kg), and significant elevation of serum concentrations of urea nitrogen (69.8 v.s. 61.7 mg/dl, 75.3 v.s. 71.5 mg/dl), Cr (11.2 v.s. 10.4 mg/dl, 10.5 v.s. 10.2 mg/dl) and UA (7.5 v.s. 7.0 mg/dl, 7.8 v.s. 7.5 mg/dl) were found in comparison to those during usual weekends. Christmas food enriched in fat elevated serum concentrations of P (5.8 v.s. 5.3 mg/dl) and K (5.06 v.s. 4.95 mEq/l) significantly, although P and K intake were not increased. The New Year food was characterized by significant enrichment of NaCl (10.0 v.s. 7.7 g/day) and water (2,130 v.s. 1,650 ml/day), whereas calorie and fat were less compared to usual diet. Serum Na concentration (141 v.s. 139 mEq/l) was significantly elevated after the New Year. Japanese Christmas food generally consists of eggs, meat, fish, squid and shells. Increased intake of P and K resulted in the elevation of serum levels of urea nitrogen, Cr, UA, P and K. Special food for the New Year characterized by salt-rich ingredients subsequently followed by much water accumulation resulted in increase of body weight. Patients undergoing maintenance hemodialysis should pay attention to the diet during Christmas and the New Year, especially on weekends.

THE RELATIONSHIP OF SERUM ALBUMIN TO SERUM PREALBUMIN IN THE DIALYSIS PATIENT

Jen Strong, Les Spry, Alison Steiber, Teresa Gerbeling, Jackie Carder
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Serum albumin (alb) is widely used as a marker of nutritional status in the dialysis patient (pt) but it has been suggested that serum prealbumin (prealb) may be a more sensitive indicator. The K/DOQI Nutrition Guidelines recommend an alb $\geq$ the lower limit of the normal range and a pt with a prealb < 30 mg/dL should be evaluated for protein-energy malnutrition (PEM).

To determine the relationship between alb and prealb, a longitudinal study of dialysis pts' monthly lab data was conducted at a midwestern dialysis facility. Data sets were analyzed only if all of the following data were available: alb, prealb, age, sex, modality and ESRD etiology. The final review consisted of 3601 data sets. The alb was measured using bromocresol green and prealb by immunoturbidimetric techniques. Alb levels were divided into 4 categories (see table).

Alb Category	< 2.50	2.51-3.50	3.51-4.00	$\geq$ 4.01
Population %	0.6	25.9	52.0	21.4
Prealb mg/dL avg	19.1	20.7	26.3	32.0
95% CI	15.4-22.8	20.2-21.2	26.0-26.7	31.4-32.6
Total data sets	22	934	1873	771

The following description applies to the data sets analyzed: 49% were female; mean age 65$\pm$16 (SD) yrs; mean alb 3.76$\pm$0.4 (SD); mean prealb 26$\pm$8.8 (SD); 82.3% in-center hemodialysis, 11.3% peritoneal dialysis and 6.4% home hemodialysis. The alb and prealb were positively correlated and both were negatively correlated with age($p<.01$). There was a significant difference in mean prealb between the alb categories ($p<.001$). The alb category was a stronger predictor of prealb level than was age, gender, modality or etiology ($p<.001$).

Although K/DOQI recommends using a prealb of < 30 as an indicator of PEM, we found a prealb >26.0 to be associated with an alb level in the normal range for our current lab provider. Therefore in addition to an alb within the normal range, a prealb >26 is an indicator of adequate nutritional status. Clearly more research is needed to determine what range of prealb is associated with optimal pt outcomes.

SERUM PREALBUMIN IN THE DIALYSIS POPULATION

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Serum prealbumin (prealb) has been used in dialysis patients (pts) as a marker of nutritional status. The K/DOQI Nutrition Guidelines recommend evaluating pts for protein-energy malnutrition (PEM) when prealb is < 30mg/dL. A longitudinal study of dialysis pts' monthly lab data was conducted at a midwestern dialysis facility to evaluate differences in prealb between modality, ESRD etiology and albumin (alb) levels. Data sets were analyzed only if all of the following data were available: alb (bromocresol green), prealb (immunoturbidimetric), age, sex, modality and ESRD etiology. The final review consisted of 3601 data sets.

	% of data	Mean Prealb mg/dL ± SD
ESRD Etiology		
Diabetes (DM)	49	25.0 ± 8.5
Hypertension (HTN)	15.5	25.4 ± 7.6
"Other" Etiology	37.7	27.7 ± 9.5
Modality		
Home Hemodialysis (HH)	6.4	31.5 ± 13.5
Peritoneal Dialysis (PD)	11.3	27.0 ± 8.3
In-Center Hemodialysis (ICH)	82.3	25.5 ± 8.3
Albumin Level g/dL		
≤2.5	0.6	19.1± 8.4
2.51-3.50	25.9	20.7± 7.7
3.51-4.00	52	26.3± 7.8
≥4.01	21.4	32.0± 8.6

The following description applies to the data sets analyzed: 49% were female; mean age 65±16 (SD) yrs; mean alb 3.76±0.4(SD); and mean prealb 26±8.8 (SD). Pts with DM and HTN as ESRD etiology had significantly lower prealb levels than did the category for "other" etiology ($p<.05$). The mean prealb was significantly different between modalities ($p<.05$) and albumin level ($p<.001$). An alb within normal range correlated with a prealb of 26.0. This data suggests that normal prealb levels for DM and HTN may be slightly lower than all other patients and less than the K/DOQI goal of >30mg/dL.

SEVERE HYPERCALCEMIA IN A HEMODIALYSIS PATIENT

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The patient is a 54-year old woman with end stage renal disease from polycystic kidney disease status post bilateral native nephrectomies. Her other significant co-morbidities include hypertension, anemia, chronic pseudomonas infection of abdominal wall, and psoriasis. She had been on hemodialysis for three months after a failed renal transplant and later a transplant nephrectomy, when it was noted that she had asymptomatic hypercalcemia with corrected total serum calcium of 13.3 mg/dL and serum phosphorus of 5.6 mg/dL. Her serum intact PTH was suppressed at 12 pg/mL (normal 15-65 pg/mL). Laboratory studies a month prior had demonstrated corrected serum calcium and phosphorus levels of 10.2 mg/dL and 3.8 mg/dL, respectively. Further work-up revealed normal PTH related peptide level. Serum protein electrophoresis was negative for paraproteins. The 1, 25-dihydroxy vitamin D3 level was 53 pg/mL (normal 22-67 pg/mL) and 25-hydroxy vitamin D3 level was 44 ng/mL (normal 25-80 ng/mL). She was not on any oral calcium preparations or vitamin-D analogs. Her calcium bath at dialysis was decreased to 2 meq/L. The following month, her corrected serum calcium was down to 11.5 mg/dL, but serum phosphorus was now 8.5 mg/dL. A month later, she was admitted with an episode of generalized tonic clonic seizures and her corrected serum calcium was 15.1 mg/dL. She was placed on a 1.5 meq/L calcium bath and was treated with phenytoin. An extensive work-up for malignancy was negative. On reviewing her medications during the hospitalization, it was noted that she was using topical calcipotriene cream, a vitamin D3 analog for her psoriasis. The topical agent was discontinued and with dialysis against a low calcium bath, her serum calcium normalized over next three months.

Topical calcipotriene is commonly used for the treatment of psoriasis and is usually well tolerated. Cases of mild hypercalcemia with its use have been reported. Patients with end stage renal disease with suppressed PTH levels are at risk for hypercalcemia. They are unable to excrete calcium through urine and their bones cannot buffer excess serum calcium due to low bone turnover. This case report illustrates that the use of topical calcipotriene in such patients can cause life-threatening hypercalcemia.

QUOTIDIAN SHORT HOME HEMODIALYSIS; COMPARING TWO TECHNIQUES AT THE DIALYSIS CENTER OF LINCOLN

L Spry, M Buss, M Carver, and J Carder. Lincoln, NE, USA

Our first patient was sent home with the Aksys PHD system in August 2003. We sent our first patient home on the NxStage System One in April 2005. As of November, 2006, we have trained 40 patients. Twenty-two patients have trained with Aksys and 18 trained with NxStage. Fifteen (68%) remain on Aksys with mean follow-up of 18 months and 11(61%) remain on NxStage system at mean follow-up of 12.6 months. Aksys patients have a mean age of 57.9 and are 57% female. NxStage patients have a mean age of 60.7 and are 75% female. Six patients (15%) are incident patients and 85% are prevalent patients converted to home hemodialysis. One patient failed training on NxStage device, 4 were transplanted, 5 returned to in-center dialysis, and 4 died. Twenty-five percent of patients started with graft access, 12.5% catheters and 62.5% primary AV fistulas. Button-hole technique was used for all fistulas. One graft and 1 fistula have been lost. Mean Epo dose increased from time of training (22,000 units weekly) to last recorded dose (26,000 units weekly). Patients dialyze 6 days per week. Nutritional status was not different between techniques.

Patients completing at least four months of therapy had quality of life measured by SF-36 inventory, and showed a slight decrease in mental component summary (MCS) scores for both techniques. Aksys patients' Physical Component Summary (PCS) scores increased from 33.53 to 38.52 ($p < 0.01$) and NxStage declined from 33.73 to 31.26 (NS). The difference between the PCS for Aksys vs. NxStage was also significant ($p < 0.01$). Mean scores for our in-center patients' MCS and PCS are 51.73 and 34.67, respectively, peritoneal dialysis patients are 49.16 and 33.35, and home hemodialysis are 51.14 and 36.03. MCS scores among all patient groups were not significantly different. KT/V for Aksys patients averaged 0.87 and NxStage averaged 0.57, and were statistically different ($p< 0.01$). Seven of 15 patients on Aksys are employed versus 4 of 11 of the NxStage patients. Eighty-five percent of Aksys and 92% of NxStage patients are from rural settings.

We conclude that home hemodialysis is a successful mode of therapy using both systems, but patients on the Aksys PHD system self-report better physical component scores on the SF-36 inventory.

TREATMENT WITH ORAL PARICALCITOL REDUCES TOTAL AND BONE-SPECIFIC ALKALINE PHOSPHATASE IN DIALYSIS PATIENTS.

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Elevated alkaline phosphatase (ALP), a common marker of bone turnover, has been shown to promote skeletal and extra-skeletal calcification via reduction in pyrophosphate levels. Normalizing ALP is associated with correction of bone turnover and lower ALP has been associated with decreased all-cause mortality in hemodialysis patients.

We conducted a series of 12-week, randomized, double-blind, placebo-controlled studies to investigate the effects of treatment with oral paricalcitol (Zemplar®), a selective vitamin D receptor activator, on ALP and bone-specific ALP (BAP) in dialysis patients with elevated parathyroid hormone.

A greater proportion of patients treated with paricalcitol experienced shifts from elevated to normal reference levels of ALP and BAP compared with placebo (Table 1). The distribution of changes in ALP and BAP from baseline to final visit is listed in Table 2.

Table 1. Change in ALP and BAP from Baseline to Final Visit

	ALP		BAP	
Categorical Shift, n (%)	Paricalcitol (n=162)	Placebo (n=137)	Paricalcitol (n=156)	Placebo (n=128)
High → Normal	30 (18.5%)	4 (2.9%)	45 (28.8%)	5 (3.9%)
Normal → Normal	108 (66.7%)	75 (54.7%)	63 (40.4%)	38 (29.7%)
Normal → High	2 (1.2%)	23 (16.8%)	3 (1.9%)	18 (14.1%)
Low → Normal	0	0	1 (0.6%)	0
Normal → Low	0	0	0	1 (0.8%)

Table 2. Distribution of Change in ALP (IU/L) and BAP (µg/L) from Baseline

		Mean	Max	q75	q50	q25	Min
ALP	Paricalcitol (n=162)	–25.7	35	–3	–19	–37	–201
	Placebo (n=137)	19.4	155	34	13	0	–62
BAP	Paricalcitol (n=156)	–12.0	15	–3	–8	–17	–99
	Placebo (n=128)	6.6	59	12	3	–2	–16

The ability of paricalcitol to decrease and normalize circulating levels of ALP and BAP is consistent with published clinical studies, and could be associated with a reduction in the risk of bone complications and mortality in dialysis patients.

EVALUATION OF THE NUTRITIONAL STATUS ACCORDING TO ESSENTIAL AMINO ACID INTAKE IN HEMODIALYSIS PATIENTS

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The mortality and morbidity rate of hemodialysis patients (HD) remain high. Among many factors, protein and calorie malnutrition has been shown to be a major risk factor for increased mortality in the HD patients population. The recommended intakes are 1.2g/jg/day for protein, and 30~35 kca/kg/day for energy. However, most of the studies published food intake in diaysis patients is usually insufficient. Malnutrition can be caused by insufficient amino acid intake, increased energy expenditure, nutrient losses in dialysate, oxidant stress, metabolic acidosis and muscle catabolism. In this study, we evaluated the association of markers of nutritional status and essential amino acids intake in HD patients. We investigated nutritional status of 41 HD patients (mean age: 64.2±11.5y, men: 24, women: 27) by measuring anthropometric, biochemical parameters and food intakes by using 24hr recall methods. Dialysis adequacy (Kt/V) was 1.17±0.17 and urea reduction rate was 67.8±6.50. Subject's total energy intake and total protein intake were 1648.0±397.31kcal/day (28.8±5.82kcal/kg/day), 79.2±27.2g/day (1.38±0.41g/kg/day), respectively. The animal protein intake was 42.7±22.1g/day, essential amino acid intake was 23.4±9.92g/day, and the ratio of essential amino acids to total protein intake was 29.6±5.42%. There were significantly positive correlation between muscle mass and lean body mass with serum creatinine level ($r=0.435$, $p<0.01$; $r=0.435$, $p<0.01$). There were also significant positive correlation in muscle mass and lean body mass with pre hemodialysis blood urea nitrogen (preHD BUN) ($r=0.329$, $p<0.05$; $r=0.329$, $p<0.05$). There were no significant correlation in total energy intake and total protein intake per kg ideal body weight (IBW) to muscle mass and lean body mass. However, there were significantly positive correlation between the ratio of essential amino acids and muscle mass and lean body mass ($r=0.368$, $p<0.05$; $r=0.405$, $p<0.01$). And serum hematocrit concentration was positively correlated with the ratio of essential amino acids ($r=0.032$, $p<0.05$). The results of this study indicate that strong associations exist in essential amino acid intakes with malnutrition than total protein intakes in HD patient. In conclusion, specialized nutrition education should be necessary to efficiently improve the quality of protein intakes.

DIALYSIS DOSE DELIVERY IN HOSPITALIZED PATIENTS WITH ACUTE KIDNEY INJURY

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Intermittent hemodialysis (IHD) is the most common modality for renal replacement in hospitalized patients with acute kidney injury (AKI). Dosing guidelines for IHD in outpatient ESRD patients require a minimum Kt/V of 1.2. Currently there are no established guidelines for dialysis dosing for in-hospital patients and it is unknown if the same Kt/V criteria are applicable for hospitalized AKI patients. We retrospectively analyzed data on patients who underwent in-patient dialysis for AKI over a 12 month period to evaluate the prescription and delivery of IHD estimated from derived Kt/V (Daugirdas JT: Second generation logarithmic estimates of single-pool variable volume Kt/V: An analysis of error. *J Am Soc Nephrol* 4:1205-1213, 1993). A polysulfone membrane (Fresenius F60NR) was used for all sessions and URR was calculated from pre and post dialysis urea nitrogen levels. One hundred and thirty three patients had 748 IHD sessions during this period. 27% of the sessions were in an ICU setting. Vascular access included tunneled catheters in 61% and non-tunneled in 39%. Heparin was used for anticoagulation in 35% of the sessions and saline flushes in the remainder. Delivered dialysis duration was 3.3 hours. Of the 748 HD sessions, overall mean Kt/V was 1.42. A low Kt/V (<1.2) was seen in 32% of the sessions

In 98 % of the sessions dialysis duration matched that prescribed. Factors associated with a low Kt/V were fewer minutes of HD treatment delivered (204 min vs. 186 ;p=0.0001), use of non-tunneled catheters vs. tunneled (p=0.002), ICU location vs. non-ICU (p=0.0006), low blood flow rates (303 vs. 341; p<0.0001)and access problems during dialysis (28% vs. 12% without access problems, p<0.0001). Anticoagulant type and net ultrafiltration did not influence low Kt/V.

Conclusions: Kt/V is an easy measure of dialysis delivery in hospitalized AKI patients on IHD. Low Kt/V was seen in about 1/3 patients and was more prevalent in non-tunneled venous catheters, low duration of dialysis and access problems. Tunneled catheters should be the preferred vascular access. Future research to define parameters for dose adequacy in ARF could focus on tunneled catheter and increased dialysis time. URR can be a measure to help modify dialysis prescription and delivery in hospitalized patients.

INTRADIALYTIC PARENTERAL NUTRITION (IDPN): CHANGES IN ALBUMIN, TOTAL PROTEIN, DRY WEIGHT, BUN, AND CREATININE AFTER 3 TO 12 MONTHS OF THERAPY.

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An observational, retrospective study of response to IDPN was conducted in 164 maintenance hemodialysis (MHD) patients (pts) who received the therapy for 3 to 12 months over a 46 month period in 28 different dialysis units. Data was gathered from dialysis unit medical records. At the start of therapy mean age was 63.3 years with a range of 22 to 91 years, 47% male, 53% female and 52% had diabetes. All pts received amino acids (average 58.5 g/treatment) and dextrose three times a week during MHD. In addition 16% of pts received 10% lipids and 63% of pts received 20% lipids at each treatment in a 3 in 1 solution. Lipid intolerances were reported in 8 pts (5%), 5 had nausea and/or vomiting and 3 unspecified symptoms. In 9 of 164 pts (5%), IDPN was stopped because of intolerance not related to lipids.

In 147 pts with complete data, mean baseline albumin (ALB) was 2.7 gm/dl (range 1.3 to 4.4) and mean final ALB was 3.1 gm/dl (range 1.3 to 4.6). Mean ALB change was +0.4 gm/dl. An improvement in ALB of at least 0.3 gm/dl was observed in 59% of pts. In 126 pts with complete data, mean baseline total protein (TP) was 6.6 gm/dl (range 4.1 to 11.0) and mean final TP was 7.1 gm/dl (range 4.6 to 11.3). An improvement in TP of greater than 0.2 gm/dl was seen in 60% of patients. Mean weight change in 138 pts with complete data was -1.5 kg (range of -20.5 to +10 kg). Fifty percent of pts lost weight, 16% maintained weight and 34% gained weight. In 146 pts with complete data, mean baseline BUN was 40 mg/dl, mean final BUN was 52 mg/dl and mean BUN change was +12 mg/dl. BUN improved by at least 20 mg/dl in 36% of pts. In 144 pts with complete data, mean baseline creatinine (CR) was 6.5 mg/dl and mean final CR was 6.6 mg/dl.

In conclusion IDPN was well tolerated and resulted in positive responses in ALB, TP and BUN in the majority of pts. Epidemiological studies have shown that improvement in ALB of the magnitude seen in our study results in a marked improvement in survival and morbidity in MHD pts. IDPN appears to be an effective therapy for raising ALB levels in MHD patients with protein malnutrition.

A SIMPLE FEEDBACK TOOL TO ENHANCE PATIENT EDUCATION ON ADVANCE DIRECTIVES

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Using a short self report form to solicit patient feedback after providing education and counseling on Advance Directives has doubled our measurable results and has served as an icebreaker for discussion on this sensitive topic.

Previous attempts to increase our dialysis patients' understanding of Advance Directives through social work education and counseling did increase the number of patients with written Advance Directives from approximately 4% to 18% of our patient population. In addition to individual teaching and counseling, we provided patients with fact sheets and brochures, placed Advance Directives information in the patient areas, put up question and answer bulletin boards, and held patient support group discussions on end of life issues.

In 2006, we continued to use these methods, but with one addition. After social workers counseled patients about Advance Directives, they asked the patients to fill out a short (1/3 page) written checklist. The purpose of the checklist was to solicit the patients' responses to the information presented and to allow the patients to state their wishes about Advance Directives. Patients were given these choices: (1) I have an Advance Directive on file that expresses my current wishes, (2) I have one at home, (3) I want further information, (4) I am considering writing an Advance Directive, or (5) I am not interested in having an Advance Directive at this time. Space was included for comments.

Since we have asked patients to give a brief, but formal response to the education we provide, we have seen an increase in the number with written Advance Directives to over 30% of our population. Patients who filled out checklists were more likely to seek information on Advance Directives, engage in discussions of end of life planning, and to complete or to update an existing Advance Directive.

This simple tool requires patients to take an active role in education, and provides the facility with a concrete documentation on patient education without the staff having to do more paperwork.

NEPHROGENIC FIBROSING DERMOPATHY IN A PATIENT WITH MULTIPLE MYELOMA AND BONE MARROW TRANSPLANT.

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Nephrogenic fibrosing dermopathy (NFD) is a newly emerging disease entity that has manifestations similar to scleromyxedema. NFD first began appearing in literature in 2000 and is found in patients with chronic renal insufficiency, most of whom had undergone hemodialysis, peritoneal dialysis or renal transplant prior to onset. The pathogenesis of NFD is still unclear, but is proposed to be the result of circulating fibrocytes being recruited to the skin in response to several signaling molecules. Here, we report the case of a patient with a history of multiple myeloma, which developed acute renal failure and subsequently received bone marrow transplantation. The circulating fibrocytes involved in NFD are thought to originate from the bone marrow, and the transplant may have played a role in the development of this patient's condition. In this case report, we review some of the literature on the manifestations, pathogenesis, and treatment of NFD.

EFFECTIVENESS OF ULTRASONOGRAPHY VEIN MAPPING FOR THE CREATION OF AV FISTULA

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AV fistula is the preferred access in HD patients. The prevalence of AV fistulae is about 75-80% in Europe and Canada but in USA, is still less than 40%. There are various reasons for this situation. One major contributing factor is the preoperative exclusion of potential candidates if an adequate vein is not found by evaluation with ultrasound venous mapping. We wanted to find out just how effective ultrasound venous mapping criteria are in the creation of a successful viable AV fistula.

We have evaluated 5 patients who were initially excluded by ultrasound venous mapping, but had undergone AV fistula access surgery regardless, as per the patients' wishes to attempt to lower infection rate. The patients were all African American, two male, three female, age ranging from 31 to 76 years, with all five having hypertension, and two being diabetic. The US venous mapping showed no vein at all in two of the patients and inadequate vein in three of the patients. All of the patients received radio-cephalic AV fistulae.

All of the patients received follow up in at least six weeks with successful development of fistulae in all five of the patients.

Ultrasound venous mapping does not always correctly predict the creation of successful AV fistulae in dialysis patients, and its use as the predominant screening tool may possibly need to be reevaluated.

VASOPRESSIN RESPONSE IN INTRADIALYTIC HYPOTENSION

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Intradialytic hypotension (IDH) is a major complication seen during hemodialysis and is associated with increased morbidity/mortality. Sodium modeling, cooled dialysate, and midodrine are used with varying tolerability and associated risks. Arginine vasopressin (AVP), an endogenous hormone that acts as a vasopressor, may be insufficiently secreted during episodes of IDH. Presently, there are no studies comparing AVP levels during dialysis in patients with and without IDH.

We performed a prospective, observational study of 20 chronic hemodialysis patients evaluating baseline AVP level and AVP trend during ultrafiltration in patients with and without IDH. Ten IDH patients and 10 controls were enrolled and matched for age, gender, dialysis vintage, and diabetic status. Inclusion criteria: documented IDH (3 episodes of SBP fall > 20mmHg to level < 100mmHg in 50% of dialysis treatments over 1 month) or control patients without hypotension, stable dry weight, age > 18 years old. Exclusion criteria: patients in their first 3 months of dialysis, active illness, unstable dry weight. All patients were dialyzed on a stable sodium bath with no other changes in the prescription. Blood pressure was monitored every half-hour throughout treatment. AVP levels were obtained at the start of dialysis and every hour thereafter including at completion. Samples were also taken during hypotensive episodes. Measurements were evaluated in two separate dialysis treatments.

We speculate that IDH patients will have baseline AVP levels similar to control patients but will demonstrate smaller increases in AVP during ultrafiltration suggesting an inadequate AVP response to hypotension compared with control patients who may reveal stable or increased levels of AVP during dialysis with ultrafiltration. This study may provide insight into the mechanism of IDH due to the lack of appropriate vasopressin response in the setting of hypotension. This may provide a target for future clinical interventions for IDH. Final results of the study will be available for the NKF 2007 Spring Clinical Meeting.

SERUM FRUCTOSAMINE (SF), AN ALTERNATIVE MARKER OF GLYCEMIC CONTROL, PREDICTS HOSPITALIZATION AND INFECTION IN DIABETIC HEMODIALYSIS (DMHD) PATIENTS (PTS) BETTER THAN HEMOGLOBIN A1C (HBA1C)

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Diabetes is the leading cause of end stage renal disease (ESRD) and is known mortality risk in HD pts. We have previously reported that SF may offer advantages over HbA1c as an alternative index of glycemic control in DMHD pts. The objective of this study was to examine the association of SF and HbA1c with morbidity and mortality in this population. We enrolled 100 DMHD outpatients treated at the Long Island College Hospital beginning in February 2005, and followed them for 15-21 months. Demographics, biochemical and clinical data including hospitalization and episodes of infection were recorded. HbA1c levels were measured by an immunoturbidimetric method. SF level was measured by a colorimetric method and was corrected for the concentration of serum albumin. The mean age was 63 years. Fifty-four percent were women, and the majority were African-American (72%). Mean corrected SF and HbA1c were 977±231 (SD) μmol/g (range: 607-1994) and 7.3±1.7 (SD) % (range: 5-13.2), respectively. Pts who were hospitalized during the study period had higher levels of SF (1015 vs. 824 μmol/g, $p<0.0001$) but similar HbA1c (7.31 vs. 6.88%, $p=0.24$) compared to those who were not hospitalized. Pts (excluding those dialyzed via vascular catheters) with episodes of infection had higher corrected SF (1034 vs. 885, $p=0.003$), and HbA1c (7.65 vs. 6.75%, $p=0.03$). Corrected SF, but not HbA1c, was directly correlated with rate of hospitalization ($r=0.52$, $p<0.0001$), and number of hospital days ($r=0.35$, $p=.009$). SF ($r=0.41$, $p=.003$) and HbA1c ($r=0.29$, $p=0.03$) were directly correlated with number of episodes of infection in pts with AV access. Lower tertiles of SF had better survival, but the difference did not reach statistical significance. In summary, enrollment corrected SF, an alternative index of glycemia control, was more closely associated with hospitalization and infections in diabetic HD pts than HbA1c. The clinical significance of these findings needs to be confirmed in large prospective trials.

MENTAL SCORE IS BETTER THAN PHYSICAL SCORE IN A HEALTH SURVEY OF DIALYSIS PATIENTS

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The usefulness of the SF-36 health survey instrument in estimating disease burden is widely used. SF-36 measurement tool is now used in hemodialysis patient. The questionnaire reflects perceived present health condition, comparison of health status to 1 year ago, short term or last 4 weeks account of the lists of activities during a typical day, range of problems due to physical or emotional problems and their effects on social and family life, body pain and its effect in the normal activities, overall feelings and its effect on physical and emotional health, and lastly a statement about the perception of one's health situation. All the above were placed in three categories. Physical Component summary (PCS) correlates with physical functioning, role-physical, and body pain scales. Mental component summary (MCS) correlates with Mental health, role-emotional and social functioning scales. Mental health (MH) scale include nervousness, down in dumps, peaceful, sad and happy. The vitality, general health and social functioning scales correlates with both PCS and MCS.
Thresholds below 52 in MH, 32 in PCS 34 and 42 in MCS correlates significantly with morbidity and mortality in general population.

SF-36 survey questionnaire was given to patients in an urban dialysis unit. Average age 57 years, F:M 64:46, 40%diabetics, 10% amputee and total number surveyed was 92 patients. The social worker of the unit also compared her own personal observation with SF-36 results.

SF-36 results revealed that 80.4%0(74/92) of patients has higher Mental Health (MH) scale (More than 52), 72.8% (67/92) has higher Mental component summary (MCS) score (More than 42) but only 43.3 %(39/92) of the same group has higher Physical component summary (PCS) score.

The SF-36 survey in dialysis patients reveals that mental component or MH and MCS have better score than physical or PCS score. A detail survey may be needed to explore the difference and the complex interaction between Mental and physical score in dialysis patients.

CAN ORAL SUPPLEMENTATION WITH A COLLAGEN-CASEIN BASED HYDROLIZED LIQUID PROTEIN IMPROVE SERUM ALBUMIN LEVELS IN HYPOALBUMINEMIC HEMODIALYSIS PATIENTS?

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Decreased albumin (ALB) synthesis results in hypoalbuminemia and occurs due to the interrelationship of inflammation and malnutrition (uremic malnutrition) observed in chronic hemodialysis (CHD) patients. Improving the nutritional status of CHD patients is necessary to prevent and treat uremic malnutrition. The issue remains in *how* to achieve this goal in CHD patients given the barriers to adequate and appropriate intake such as anorexia, dietary restrictions and impaired nutrient absorption. The objective was to determine if oral supplementation with a collagen-casein based hydrolyzed liquid protein can improve ALB in hypoalbuminemic CHD patients.

Our subjects were adult CHD outpatients with serum ALB > or =2.8 g/dL and < or =3.7 g/dL with given written consent.

Subjects (age = 31-90y) were divided into 2 groups based on days of dialysis. Controls (n=21; dialysis days TThSat) received standard nutritional counseling. Study group (n=29; dialysis days MWF) received 30 ml of liquid protein one hour into and 15 minutes before the end of treatment. The main outcome measures included: Baseline and monthly ALB for 3 months and subjective assessment of adverse events.

In the control group, 5 subjects did not complete the study (final n=16 [49%]) and 12 subjects in the study group, (final n=17 [51%]). There was not a statistically significant correlation between baseline ALB and baseline CRP, r= -0.30 (P=0.093) or between baseline ALB and baseline URR, r= 0.27 (P=0.14). There was no difference in the average ALB between baseline (3.43) and final (3.44 g/dL) for the control group, t= -0.54; df=15; P=0.60. In the study group, the final average (SD) ALB (3.73 [0.28]) was statistically significantly greater than baseline (3.49[0.20]), t= -4.19; df=16; P=0.001.

These statistically significant results indicate that oral supplementation with a collagen-casein based hydrolyzed liquid protein can improve serum albumin levels in hypoalbuminemic CHD patients.

BLOOD VOLUME MONITORING IMPROVES VOLUME ASSESSMENT AND MANAGEMENT AS DETERMINED BY CARDIOVASCULAR PARAMETERS.

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Both over and under hydration have been associated with intradialytic morbidity, long-term cardiovascular complications and death.

We hypothesized that the effective use of the Hct-Guided Blood Volume Monitoring algorithm (BVM) does improve UF optimization as determined by cardiovascular outcomes.

A prospective observational study in 33 hemodialysis (HD) patients, comparing clinical data pre and post nurse training, in the effective use of the Hct-Guided BVM algorithm was conducted. Patients age >18 years, after at least three months of starting HD, on thrice weekly HD were included.

(BVM) algorithm removed the first 50% of total ultrafiltration (UF) in the first hour of HD and the second 50% of UF target over the remaining time:

Hct-Guided BVM algorithm: 1) Improved blood pressure profile (2) Decreased BP medications (3) Decreased dialysis-associated events (4) Increased patients with Hct at target (5) Reduced hospitalizations(6) Reduced volume related hospital stay.

Outcome measurements		Pre-intervention			Post-intervention			P-value
		N	mean	SD	N	mean	SD	
Cardiac function	Predialysis SBP	33	154.69	15.99	33	120.96	14.06	<0.001
	Predialysis DBP	33	84.69	11.78	33	76.79	10.99	<0.001
	Predialysis Pulse Pressure	33	70.36	18.88	33	44.88	8.86	<0.001
	Postdialysis SBP	33	148.82	19.78	33	119.63	8.13	<0.001
	Postdialysis DBP	33	84.24	12.26	33	71.41	8.28	<0.001
	Postdialysis Pulse Pressure	33	64.58	18.23	33	48.12	11.12	<0.001
	Medications	33	3.06	1.58	33	1.32	1.01	<0.001
Adverse events	Hypotensive episode	33	0.7	0.74	33	0.12	0.28	<0.001
	Hypotensive episode	33	0.7	0.66	33	0.05	0.15	<0.001
	Dizziness on dialysis	33	1.39	0.92	33	0.32	0.49	<0.001
Nutrition status	albumin	33	3.29	0.57	33	3.38	0.41	<0.001
	ferritin	33	380.6	267.03	33	306.27	179.51	0.1
	Epocoitin	33	17.33	16.39	33	9.55	7.84	<0.001
	Hemoglobin	33	10.15	1.18	33	11.75	1.21	<0.001
	Predialysis Hematocrit	33	30.49	3.47	33	35.28	3.62	<0.001
	Postdialysis Hemoglobin	33	12.07	1.20	33	13.61	1.22	<0.001
	Postdialysis Hematocrit	33	36.2	3.6	33	40.82	3.66	<0.001
Hospitalization	Hospitalization	33	0.27	0.57	33	0.06	0.24	0.033
	Hospital days	33	2.27	6.29	33	0.18	0.69	0.066

Are these good short term outcomes attributable to the proper use of algorithm, or to better follow-up in these patients? This question remains to be tested in a randomized prospective controlled trail.

HIGH DOSE PARICALCITOL THERAPY USED TO DECREASE iPTH > 4000 pg/ml

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Controlling iPTH and avoiding parathyroidectomy are important in managing the care of the hemodialysis patient. Patients who are compliant with their oral medications and diet may benefit from high dose paricalcitol therapy.

We report a case of a 74 year old female patient with a peak iPTH of 4150. This patient had many co-morbidities and avoiding parathyroidectomy was an important consideration in her care. The patient had been on 10-14mcg paricalcitol for 9 months. The lowest iPTH attained during this time period was 1355. With much discussion it was decided to increase the dose to a maximum of 40mcg/treatment. The patient was also on Sensipar during this time period. The paricalcitol dose was increased from 25mcg to 40mcg over a 3 month period and the patient was maintained on a dose of 40mcg for 6 months. Her iPTH dropped from a maximum of 4150 to 260. At this point, the paricalcitol dose was decreased to 35mcg for 1 month, 25mcg the following month, and finally 10mcg. The patient's iPTH dropped to 161. The patient's calcium level remained <10.0 until the last 2 months, when it reached a level of 10.1. The patient had a maximum alkaline phosphatase of 591, which dropped to 101 during this time period.

Prior to the high dose paricalcitol therapy, the patient reported breaking ribs when bending over, mid-abdominal pain and fatigue. During the time period of the high dose therapy and decreased iPTH level, her symptoms improved. She experienced improved endurance, lessened mid-abdominal pain and no bone fractures. She is very pleased with the result of this therapy.

In summary, this demonstrates that high dose paricalcitol therapy may be a choice to avoid parathyroidectomy in patients who are compliant with their medications and their low phosphorus diet restrictions.

EARLY DETECTION OF ARTERIOVENOUS FISTULA STENOSIS BY DOPPLER ULTRASONOGRAPHY (DUS)

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A substantial proportion (20-50%) of new dialysis fistulas are not usable for dialysis due to failure to mature. Early stenosis near the anastomosis or in the draining vein occurs commonly in immature fistulas, and correction of the stenosis may promote fistula maturation. Stenosis may be detected by a fistulogram (invasive and expensive) or by DUS (noninvasive and cheap). However, little is known about the accuracy of DUS in predicting stenosis in clinically immature fistulas.

We queried a prospective, computerized vascular access database to identify 59 patients undergoing DUS within 2 months of fistula creation AND a fistulogram within 2 months following the DUS. Their mean age was 58 years, 56% were male, 83% were black, 58% had diabetes, 52% had an upper arm fistula, and 34% had clinical signs of fistula stenosis. A >50% stenosis on fistulogram was deemed hemodynamically significant. DUS was considered suspicious for stenosis if: (1) Systolic Velocity Ratio (SVR) >3:1 within 4 cm of the anastamosis or >2:1 in the outflow vein, OR (2) Peak Systolic Velocity (PSV) >4 m/sec at the stenosis, OR (3) access flow < 400 ml/minute.

Of 46 patients with significant stenosis by fistulogram, 41 had a positive DUS (sensitivity 89%), and 5 had negative DUS. Of 51 patients with positive DUS, 41 had stenosis by fistulogram (positive predictive value 80%). The overall accuracy of DUS was 74.5%.

We conclude that DUS is a sensitive, non-invasive tool to screen for significant stenosis in clinically immature fistulas.

INTENSIVE EDUCATION AS A QUALITY IMPROVEMENT TOOL TO REDUCE INTERDIALYTIC WEIGHT GAIN (IDWG) IN CHRONIC HEMODIALYSIS (CHD) PATIENTS

Jeanette McLaughlin; Katrina Hebert; Tammy Poma; Nicole Stankus

Background: IDWG is an important patient compliance measure in CHD setting. Large IDWG has been associated with poor patient outcomes. We assessed the impact of an intensive multidisciplinary education on reduction of excessive IDWG.

Methods: Data was collected and analyzed following a month-long intensive education which targeted all patients. It employed a broad multidisciplinary approach (nurses, dietitians, social workers, dialysis technicians and physicians) and was performed as a quality improvement initiative.

Results: Twenty-four patients (17.4%) with average IDWG greater than target of 5% of their estimated dry weight (EDW) prior to the intervention were in the excessive IDWG group (EG). All other patients were included in the target gains group (TG). After the intervention, IDWG trend was analyzed over the course of 8 months in both groups separately. Significantly smalle weight gains were noted in the EG group ($p=0.006$ at month 1, $p= 0.009$ at month 2, 0.01 at month 3, $p<0.001$ at month 4, $p=0.002$ at month 5, $p<0.001$ at months 5, 6 and 8). At the end of the intervention month 54% of the EG group continued to have excessive IDWG, followed by 58% at 2 months, down to only 32% at 4 months, 44% at 6 months and 39% at 8 months. The TG showed no change in IDWG compared to baseline, except in month 8 analyzed (increase in IDWG, $p=0.025$).

Conclusion: An intensive multidisciplinary approach aimed at reducing IDWG can result in significant and sustained decreases in average IDWG in patients with fluid noncompliance.

THE CARDIO-RENAL-ANEMIA SYNDROME (CRA) IN HEMODIALYSIS PATIENTS.

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Background : The correction of anemia was effective in the amelioration of both cardiac and renal failure.
The aim of the present work was to study the relationship between the severity of CRA syndrome in chronic hemodialysis patients and survival probability.
Patients : 444 patients on hemodialysis were followed for 5 years.

Results: A total number of 153/444, 34% patients died during the study. The median value for the severity score of the whole group of dialysis patients was 1.83. In Kaplan-Meier analysis CRA severity score was strongly associated with the mortality, $p<0.001$.The severity score was also correlated with : albumin, hsCRP, Kt/V, erythropoietin treatment, triglycerides, Hb and CaxP product ($p<0.001$ at least).In the Cox regression analysis Hb, albumin, erythropoietin treatment and CaxP product remained significant predictors of death.

Conclusions: The severity score of CRA syndrome in HD patients is an independent and very significant predictor of death. The patients with a high severity score had more hypoalbuminemia , higher inflammation markers and probably more severe renal osteodystrophy. CRA severity scoring as defined by us is an easy tool to predict outcome of dialysis patients.

COMPARISON OF PROPHYLACTIC ANTIBIOTICS IN TUNNELED-CATHETER MANIPULATION IN DIALYSIS DEPENDENT PATIENTS

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Prophylactic antibiotics play an important role in dialysis patients undergoing dialysis catheter placement through either a new or pre-existing subcutaneous tunnel. The generally used antibiotics are Ancef (Cefazolin), Vancomycin, and Levaquin (Levofloxacin). The goal of therapy is to prevent catheter infection by gram positive/skin organisms. However, patient drug allergies may prohibit the use of one or more of these antibiotics. Our goal was to compare the effectiveness of each of these antibiotics specifically for non-septic dialysis catheter manipulation.

Over a three month period 102 catheter-dependent hemodialysis patients had either newly placed tunneled catheters or a pre-existing malfunctioning tunneled catheter replaced through the same location. Patients with active signs of tunnel infection were excluded. Patients were given prophylactic antibiotic periprocedurally. Routinely 1 gm Ancef was administered, however 500 mg Vancomycin was the substitute if the patient had a history of allergy to either penicillin or cephalosporins. In those patients with a history of allergy to both vancomycin and the cephalosporin family, they received 500 mg Levaquin. Dialysis centers were called three weeks after the patient's procedure ascertain any catheter related infections.

Two patients of the 102 (0.02%) suffered from tunnel infection (redness, tenderness, discharge from the skin entry site) within the three-week cutoff. 52 of the patients received Ancef (0.51%), 33 received vancomycin (0.32%) and 17 received Levaquin (0.17%). One of the two tunnel infections was a patient that received Ancef, the other had been given Vancomycin.

There is no significant difference in effectiveness of the three antibiotics when used for prophylaxis for new or replaced tunnel dialysis catheters. The choice of antibiotic should rely upon the patient's medication allergies.

COMPARATIVE CHARACTERIZATION OF THE NEW BAXTER XENIUM 170 DIALYZER (BX)

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Optimizing performance and biocompatibility are major goals of dialyzer engineering.

In a prospective, randomized, cross-over study on 8 ESRD patients (age 63 ± 14 years) we compared Baxter Xenium (refer as BX; modified PUREMA® H membrane made of polyethersulfone (Membrana GmbH), 1.7 m^2) to 2 synthetic high-flux control dialyzers namely Fresenius Optiflux® 180 NR (polysulfone, 1.8 m^2, refer as FO) and Gambro Polyflux® 170 H (Polyamix®, 1,7 m^2, refer as GP). Solute removal was determined by instantaneous plasma clearances (K), removal rates (RR) and mass transfer into continuously collected dialysate. Biocompatibility was assessed by white blood count, C5a, myeloperoxidase and thrombin-antithrombin III. Treatment time was 240±0 min. Blood and dialysate flow rates were set at 300 and 500 mL/min, respectively.

Small solute clearances were similar for all 3 dialyzers. Compared to FO, BX demonstrated higher b2m K (39 ± 11 vs. 46±8 mL/min) and RR (44±9 vs. 62±6 %). For the larger cystatin c, K and RR for BX (46±8 mL/min; 59±7 %) were superior compared to FO (22±9 mL/min; 35±9 %) and GP (35±9 mL/min; 56±8 %). RR of IL-6 and TNFa were also highest for BX (28±20/55±12 % vs. 16±26/43±20 % (FO) and 23±22/52±16 % (GP)). The albumin loss was <300 mg per session for all dialyzers. No differences between the dialyzers were found in the biocompatibility parameters.

BX is characterized by a steeper sieving profile with higher middle molecular removal at very low albumin loss and an excellent biocompatibility. This may contribute to more adequate dialysis therapy.

EFFECT OF HEPATITIS C INFECTION ON ANEMIA IN HEMODIALYSIS PATIENTS

Anand Khurana, Mohanram Narayanan, Allan E Nickel
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Hepatitis C has been a major infectious concern among dialysis patients. The aim of this study was to assess the effect of hepatitis C infection on anemia in our hemodialysis population.

Dialysis records from 01/1999 to 11/2006 were reviewed. Forty two patients had confirmed Hepatitis C infection by positive ELISA test on 2 occasions or on 1 occasion with confirmatory PCR testing. Patients with polycystic kidney disease, cryoglobulinemia, malignancy, hematopoetic disorders including multiple myeloma, chronic infections, or active treatment with interferon +/-ribavirin were excluded. Stable patients on dialysis for > 6 months with URR >65% and < 3 missed dialysis/month were studied. Quarterly patient data including hemoglobin, iron studies, IV iron dose and Epoetin alfa (EPO) dose were obtained from retrospective chart review for a 12 month period with no major hospitalizations or surgeries. An age, sex and race matched control group of hemodialysis patients was selected using the same exclusion criteria and the above data were recorded. Fischer's exact test was used to compare group characteristics and Student's paired t test was used to compare EPO, IV iron doses and ferritin levels.

Twenty three patients were included for analysis. Seventeen were African American. The results are summarized below.

Parameter	Hepatitis C	Control	P value
Pts not requiring EPO (n=23)	3	0	0.07
Months without EPO use (n=92)	19	2	<0.001
EPO dose (Units/month)	19626	52593	0.01
EPO dose (Units/kg/month)	278	579	0.03
IV iron (mg/month)	113	125	ns
Ferritin (nanogram/mL)	610	701	ns

Hepatitis C patients had similar iron requirements but decreased need for EPO. This may be due to release of hepatic EPO as a result of chronic inflammation secondary to Hepatitis C. This needs to be studied further.

ELEVATION OF C-REACTIVE PROTEIN LEADS TO HIGHER EPOGEN DOSING AND WORSE NUTRIONAL STATUS IN HEMODIALYSIS PATIENTS

nitin khosla, sharon soroko, sam kuo, and ravindra mehta, university of california at san diego, san diego, ca usa

Though C-reactive protein (CRP) is a well known marker of inflammatory burden, the significance of CRP elevations in hemodialysis patients is still unclear. The aim of this study was to describe the change in CRP over time and the relationship between CRP and hemoglobin, epogen dose, and albumin in hemodialysis patients. A review of all the patients in a hemodialysis center that had multiple CRP measurements from 1/1/02 through 12/31/05 yielded 120 patients. For patients with more than two CRP values, the first and last measured CRP values were used. Baseline characteristics of this cohort included a mean age of 53.4±18 years, 53% male and 30% Caucasian, 29% Hispanic, and 24% African-American. CRP values changed from 2.8±3.7 at baseline to 2.5±4.1 a median of 547 days later. The table shows the correlation coefficients between the last measured CRP (normalized by using log values) and hemoglobin, epogen dose, and albumin for all patients, for those whose CRPs increased ,and for those whose CRPs decreased from the first to last measured value.

	All patients	CRP increased	CRP decreased
Final Hemoglobin	-0.40 ($p<0.0001$)	-0.54 ($p=0.0002$)	-0.22 ($p=0.07$)
Final Epogen dose	0.36 ($p<0.0001$)	0.48 ($p<0.0016$)	0.24 ($p=0.0034$)
Final Albumin	-0.64 ($p<0.0001$)	-0.76 ($p<0.0001$)	-0.52 ($p<0.0001$)

This data suggests that higher levels of CRP are associated with more difficult to manage anemia and poor nutritional status, especially in patients whose CRP increases over time. Further studies are needed to describe the clinical implications of these findings.

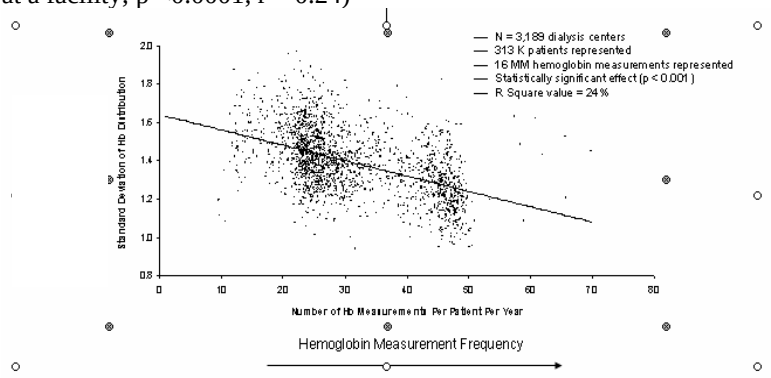
FREQUENCY OF HEMOGLOBIN (HB) MONITORING IN DIALYSIS UNITS IS ASSOCIATED WITH FACILITY-LEVEL HB VARIABILITY.

Irfan Khan and Mahesh Krishnan. Amgen Inc., Thousand Oaks, CA.

Anemia management practice patterns in dialysis show significant variation across the country. Frequency of Hb monitoring is one such practice pattern that may influence Hb variability.

We analyzed a database containing all Hb measurements recorded for 313,000 unique US patients covering the time period between Jun 29, 2003 and Jul 22, 2006. We accessed the frequency of recorded Hb values at the patient level over the entire period and then calculated an average frequency for the facility. The mean and standard deviation (SD) of Hb measurements for a facility is assessed by pooling all Hb measurements for all patients.

There were 3,189 dialysis units with an approximate range of Hb SDs between 1 and 2 g/dL. Frequency of Hb monitoring was correlated with small improvements in Hb distribution (defined as SD of all Hb values at a facility; $p < 0.0001$, $r^2 = 0.24$)



Frequency of Hb monitoring at the facility-level is inversely related to Hb variability. More frequent Hb monitoring may be one factor which allows clinicians to detect Hb changes associated with intercurrent events and patient comorbidities.

DIALYSIS PATIENTS ARE AT RISK OF BEING UNDERMEDICATED DURING HOSPITAL STAY

Charles Jere, Mehbeen Khan, Ryan Chowdhury, Monica Grafals, Karthik Ranganna, Ziauddin Ahmed
Department Of Medicine, Drexel University College Of Medicine

Dialysis therapy only can replace the filtration function of ESRD patients. Supplemental therapies are routinely prescribed to replace endocrine, metabolic and other functions of the kidneys in ESRD management. Medications including water soluble vitamins, Vitamin D or its analogues, phosphate binders, erythropoietin, IV iron are routinely used in most dialysis patients. Dialysis patients when hospitalized should have continued on these medications. We have decided to do a survey in our tertiary care teaching hospital to see how many of the hospitalized end stage renal disease patients are maintained on their out patients supplemental medications.

Twenty three hospitalized dialysis patients' charts were reviewed in an one month period. Information regarding the medication list, pertinent medical information, and laboratory values of first 48 hours of admission was noted. The reasons if any for not initiating any medications were analyzed.

Erythropoietin was given in 10/17 (58%) patients whose Hg was less than 11 Gm/L
Multivitamins were given 18/23 (78.2%) patients. In 18 patients phosphorus was more than 5.5mg/dl but binders were started in 9/18(50%) patients. Vitamin D therapy was given in 11/23 (47%) patients but since PTH level was not routinely ordered in hospitalized patients, the need could not be fully evaluated. Iron studies were recorded in 4/23 (17%) patients and could not be evaluated for the requirement of IV iron in other patients.

The hospitalized dialysis patients do not routinely receive their supplementary medications within at least first 48 hours of their admission. A larger survey may be needed to evaluate the extent and the reason of this problem.

AN INNOVATIVE APPROACH TO GLYCEMIC CONTROL IN ESRD PATIENTS (pt)

Kalyana Janga , Sheldon Greenberg , Miriam Greenberg , Saurabh Goel Subrahmanyam Nasika .Maimonides Medical Center ,Brooklyn ,NY.

Diabetes (DM) is a leading cause of ESRD in the USA.Good glycemic control is essential in the dialysis pt, to slow the progression of microvascular disease as well as protect against macrovascular disease.Achieving proper glycemic control in the Maintainence Hemodialysis (MHD) pt, however presents a unique challenge as their diets are already restricted, their medications are often numerous and they must adhere to a strict schedule of dialysis treatments. The purpose of our report is to introduce an innovative approach to improve glycemic control in MHD patients with minimal patient effort.

We describe a 72 yr old male with DM,HTN,CAD on MHD for 3 yrs , who had poor glycemic control despite therapy with maximum doses of 2 oral hypoglycemics.His glucose was >200 mg/dl fasting and >250 mg/dl prelunch.His HbA1c was 13.3.He refused administration of insulin at home.We postulated that lantus, a long acting insulin would continue to exert its affect in MHD patients until the next dialysis treatment to achieve overall desired glycemic control.Our patient agreed to take insulin at the dialysis center. We placed our patient on a regimen of lantus 3 times a week postdialysis.Lantus was begun at 5 U SQ and was progressively increased to 17 units after each dialysis session based on fasting glucose levels (measured at home) and prelunch glucose levels (measured at dialysis) After 3 months ,the blood glucose levels decreased to 100 –110 mg/dl fasting and 125-135 mg/dl prelunch. HbA1c levels decreased from 13.3 to 8.4 in 4 months and to 7.9 in 8 months duration.

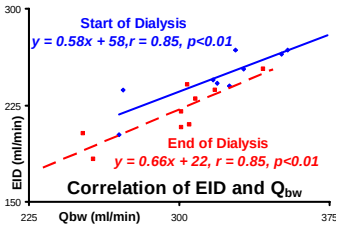
In conclusion our approach to glycemic control in MHD patients achieved good results with minimal patient effort and would be beneficial for the following population:

1. Patients with DM uncontrolled by oral hypoglycemics, who refuse to take insulin at home.
2. Patients on multiple medications for multiple medical problems,who are more prone to noncompliance.
3. Patients dissatisfied with the complexity of multiple daily insulin injections.

FACTORS RESPONSIBLE FOR REDUCTION IN EFFECTIVE IONIC DIALYSANCE (EID) DURING HEMODIALYSIS (HD).

Manasvi Jaitly, Sumit Mohan, Muhammad Mujtaba, Herman Anderson, Jen-Tse Cheng, Velvie Pogue. Harlem Hospital, NY.

Effective Ionic Dialysance calculated using changes in dialysate Na^+ conductivity is an online measure of HD adequacy. EID is measured at regular intervals by the Gambro® Phoenix dialysis system during treatment. Access recirculation (AR) and cardiopulmonary recirculation (CPR) are thought to affect EID during dialysis. We observed a ↓ in EID during HD and attempted to explain this ↓. Data were collected for 9 pts in the first and last 30 mins of treatment. We measured AR, access blood flow (Q_a), cardiac output (CO), actual blood flow (T_b) using ultrasound dilution. Compensated blood flow (Q_b) was recorded from the dialysis system. Blood and dialysate samples were obtained to calculate dialyzer clearance for urea (K_dUN) and creatinine (K_dCr). Plasma protein and hematocrit were measured to calculate the total blood water flow (Q_{bw}) and plasma water flow (Q_{pw}). A significant ↓ in the EID (247 v 221, *p<0.01*), K_dUN (280 v 228, *p<0.02*) and K_dCr (215 v 171, *p<0.01)* was noted at the end of treatment in the absence of a significant ↓ in Q_b (398 v 396, *p=ns*). However, a significant ↓ in T_b (374 v 355, *p<0.01*), Q_{bw} (319 v 299, *p<0.01*) and Q_{pw} (215 v 192, *p<0.01*) was seen. The Q_a (903 v 879, *p=ns*) and AR (0 v 0) did not change but the ↓CO (5.4 v 4.3, *p<0.01*) at the end produced a significant ↑CPR (16% v 19%, *p<0.02*). A significant *(p<0.01)* linear relationship was seen between (T_b, Q_{bw}, Q_{pw}) and (EID, K_dUN, K_dCr). We propose that ↓Q_{bw} during dialysis because of continuing UF leads to↓EID. Other causes of ↓EID may include ↑CPR and ↓dialyzer surface area (reflected by ↓EID for the same Q_{bw} towards the end of HD). The ↓Q_{bw} and ↓Q_{pw} without a significant ↓ in Q_b, underscores the importance of using T_b to assess K_d. In conclusion this study shows the contribution of ↓Q_{bw} and ↓dialyzer surface area to ↓EID during treatment.



ECHOCARDIOGRAM DIAGNOSIS OF PULMONARY HYPERTENSION MAY BE INACCURATE IN ESRD PTS

Ifeanyi Isaiah, Jesse Goldman, Sung-Ji Schmidt, Sheila Weaver, Jean Lee, Temple University Divisions of Nephrology and Pulmonary

Previous studies of PPH in hemodialysis (HD) patients suggest an increased prevalence of 26.7%-39.7%. However, these studies rely exclusively upon echocardiography to define PH and echocardiography often overestimates pulmonary arterial pressures (PAP). We applied current American College of Chest Physician (ACCP) guidelines, using right heart catheterization (RHC) to establish the true prevalence of PH

We conducted a retrospective, observational, analysis of all echocardiographic and RHC studies in prevalent HD patients from our outpt dialysis units. We used a peak systolic PAP $\geq$ 40 mmHg by 2-D echocardiogram initially to screen for PH and later a mean PAP $\geq$ 25 mmHg (with pulmonary capillary wedge pressure (PCWP) < 15 mm Hg) to confirm PPH. In subjects with PCWP >15, a trans-pulmonary gradient (TPG) > 15 suggested a mixed disease process. Patients with valvular abnormalities or Left Ventricular (LV) ejection fraction < 40% were excluded.

Medical records of 502 patients (56% female; mean age 59.4 ± 14.037 years) were reviewed. 439 patients had undergone echocardiography. 127 (28.9%) patients had an elevated PAP suggesting PH (mean PAP was 43.098 ± 11.404 mmHg). Of these patients, 22 (17.32%) also had RHC data. 11/22 (50%) of these patients had RHC confirming elevated mean PAP. PCWP exceeded 15 mm Hg in all 11 patients. 46 additional patients had RHC obtained for a variety of reasons without echo. Of these patients, 40 patients had mean PAP $\geq$ 25 mmHg. 14 of these patients had PCWP $\leq$ 15 suggesting primary disease. 26 of these patients had PCWP > 15. 16 patients had TPG $\leq$ 15 (suggesting heart failure as etiology) and 10 patients had TPG > 15 (suggesting mixed disease process therefore 10/439 or 2.3%).

Our study shows a higher prevalence of PH in ESRD pts receiving HD than the general population. However, based on RHC data, the true prevalence of primary pulmonary hypertension in these patients is overestimated by echocardiography. Therefore, we recommend that all hemodialysis patients with echocardiographic evidence for PH have subsequent RHC to determine whether PPH is actually present.

RENAL FUNCTION RECOVERY FOLLOWING VELCADE AND EXTENDED HEMODIALYSIS IN PATIENTS WITH REFRACTORY MULTIPLE MYELOMA AND CAST NEPHROPATHY: CASE STUDIES.

Colin A. Hutchison,[1] Mark Cook,[1] Stephen Harding,[2] Graham Mead,[2] Paul Cockwell,[1] Arthur Bradwell.[3] [1]Queen Elizabeth Hospital, [2]The Binding Site and [3]University of Birmingham, Birmingham, UK.

Renal impairment from free light chain (FLC) cast nephropathy is associated with significantly worse outcomes in patients with multiple myeloma (MM). Studies have shown that extended hemodialysis using a high cut-off dialyser (Gambro HCO 1100) is a safe and effective means for rapidly lowering serum FLC concentrations in patients with new MM and dialysis dependent acute renal failure (ARF).

Two patients with refractory MM, cast nephropathy and dialysis dependent ARF have now been treated in a similar manner. One patient presented a month earlier with an IgG kappa MM. He was unresponsive to initial treatment of thalidomide/dexamethasone with rising IgG and free kappa concentrations. This was associated with a rapid deterioration in his renal function (eGFR<10).

The second patient had received a bone marrow transplant two years earlier for IgG lambda MM. 6 months prior to admission he relapsed and was commenced on thalidomide/dexamethasone. Despite this serum lambda FLC concentrations continued to rise and he presented with dialysis dependent ARF.

Both patients were treated with extended hemodialysis and combination chemotherapy (Velcade, doxorubicin and dexamethasone). Dialysis using 2 Gambro HCO dialysers in series was preformed on non-Velcade days for 8 hours. Thrombocytopenia occurred in both patients following chemotherapy and regular replacement of albumin and magnesium was required to support the extended dialysis. Both patients achieved sustained reductions in serum FLC concentrations of greater than 60% and subsequently became independent of dialysis. No serious adverse events occurred.

REMOVAL OF FREE LIGHT CHAINS BY EXTENDED HEMODIALYSIS IN PATIENTS WITH CAST NEPHROPATHY: A PHASE 1/2 CLINICAL TRIAL.

Colin A. Hutchison,[1] Mark Cook,[1] Stephen Harding,[2] Graham Mead,[2] Paul Cockwell,[1] Arthur Bradwell.[3] [1]Queen Elizabeth Hospital, [2]The Binding Site and [3]University of Birmingham, Birmingham, UK.

Cast nephropathy is the predominant cause of irreversible renal failure in patients with multiple myeloma. The casts result from excess free light chains present in the serum (sFLC). Extended hemodialysis using a high cut-off dialyser (Gambro HCO 1100) was assessed for safety, efficiency and clinical outcomes for rapidly lowering sFLC in patients with new multiple myeloma and dialysis dependent acute renal failure.

Six patients received extended daily hemodialysis and induction chemotherapy (dexamethasone based regimes). Extended dialysis (2-12 hours) was well tolerated with no adverse events. Consistent reductions in sFLC concentrations were achieved during each dialysis session (45-81%). Four patients achieved a sustained reduction in sFLCs of greater than 60%. These patients subsequently became dialysis independent. Two patients did not respond to induction chemotherapy, had less sustained reduction in sFLC concentrations and remained on dialysis.

In conclusion, extended daily dialysis with a high cut-off dialyser rapidly reduced concentrations of sFLC, in patients who were responsive to induction chemotherapy. Dialysis independence occurred in patients who achieved >60% sustained reduction.

Patient	Myeloma type	FLC (mg/L)	Sustained % serum reduction achieved	Dialysis Status
1	MGUS → IgGκ	1,030	95	Independent eGFR 49 (9)*
2	New IgAκ	42,000	50	Dialysis dependent
3	New IgAκ	13,500	85	Independent eGFR 29 (4)*
4	New IgGλ	1,120	0	Dialysis dependent
5	New IgGλ	2,110	80	Independent eGFR 36 (2)*
6	New IgAλ	4,200	65	Independent eGFR 35 (1.5)*

*Time in months from last dialysis session.

MATHEMATICAL MODELLING OF FREE LIGHT CHAIN REMOVAL BY PLASMA EXCHANGE AND EXTENDED HEMODIALYSIS IN PATIENTS WITH CAST NEPHROPATHY.

Colin A. Hutchison,[1] Mark Cook,[1] Stephen Harding,[2] Graham Mead,[2] John Hattersley,[4] Neil Evans,[4] Mike Chapel,[4] Paul Cockwell,[1] Arthur Bradwell.[3]
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Cast nephropathy is the predominant cause of irreversible renal failure in patients with multiple myeloma. The casts result from the excess of free light chains present in the serum (sFLC). Plasma exchange (PE) has historically been used in an attempt to improve renal outcomes in these patients with disappointing results (Clark *et* al, Ann Int Med'05). Recent *in-vitro* and *–vivo* studies have demonstrated that hemodialysis (HD) using the Gambro HCO 1100 dialyser is an effective method of removing sFLC (Hutchison *et al*, JASN in press).

A two compartment model was devised to compare HD and PE as methods for rapidly lowering sFLC concentrations. Model simulations (Table) demonstrate that even 4hrs of HD 3 times a week was more effective than PE in rapidly lowering sFLC concentrations. The ineffectiveness of PE is because of its short duration. Eighty percent of FLCs are extra-vascular. Therefore, to rapidly reduce the total body load of FLCs a method which allows prolonged clearance of the extra-vascular compartment is required. The importance of the duration of treatment to cause a sustained reduction in sFLC concentrations is emphasised as the chemotherapy becomes less efficient (Table).

Mathematical modelling demonstrates that prolonged daily dialysis is a very effective method of rapidly reducing sFLC concentrations in patients with multiple myeloma and renal failure.

Method of FLC removal	Percentage of FLCs removed by intervention (and time, in days, to reduce from 10g/L to 0.5g/L) with different chemotherapeutic tumor killing rates (% per day).				
	100%	10%	5%	2%	0%
None	NA (14)	NA (30)	NA (52)	NA (121)	NA (*10 g/L)
PE x 10 in 10 days	40 (8)	34 (29)	25 (52)	13 (121)	4 (*10 g/L)
HD 4 hrs x 3/week	60 (7)	54 (19)	53 (31)	51 (73)	50 (*3.6 g/L)
HD 8 hrs daily	87 (3)	85 (7)	84 (14)	83 (29)	82 (*1.0 g/L)
HD 12 hrs daily	91 (2)	89 (5)	89 (8)	88 (16)	88 (*0.7 g/L)

*sFLC conc. at day 150 for simulations in which reductions to 0.5g/L did not occur.

HYPERPHOSPHATEMIA IS INDEPENDENTLY ASSOCIATED WITH SYSTOLIC AND PULSE BLOOD PRESSURE IN HEMODIALYSIS PATIENTS

Huang, CX[1], Plantinga L[2], Fink NE[2], Melamed ML[3], Klag MJ[2], Powe NR[2]. [1]Johns Hopkins/Sinai Hospital Program in Internal Medicine, [2]Welch Center for Prevention, Epidemiology and Clinical Research, The Johns Hopkins University, Baltimore, MD, USA. [3]Albert Einstein College of Medicine, Bronx, NY,USA.

Elevated serum phosphate has been shown to be associated with increased mortality in hemodialysis patients. We hypothesized that this association may be partially mediated by increasing blood pressure induced by mineral deposition in blood vessels that subsequently increases stiffness of arterial walls. We examined the relation between serum phosphate level and blood pressure in 729 incident hemodialysis patients from 79 clinics who were enrolled from October 1995 to June 1998 in CHOICE, a prospective cohort study. In cross-sectional analyses, serum phosphate was a significant predictor of systolic blood pressure (SBP) and pre-dialysis pulse pressure in multivariable linear regression models, adjusting for age, sex, race, serum albumin, CRP, IL-6, timing of nephrologist referral, diabetes mellitus (DM), baseline cardiovascular disease (CVD) and co-existing diseases (ICED) (P=0.001) at the start of dialysis. For each 1 mg/dL increase in phosphate, systolic blood pressure was higher by 2.02 mmHg. In longitudinal analyses, we used generalized estimating equations to examine the association between change in serum phosphate and subsequent change in blood pressure with a 3- and 6-month lag between measurement of serum phosphate and blood pressure rise. For each 1 mg/dL change in phosphate from 0 to 3 months, there was a 0.92 mmHg increase in SBP from 3 to 9 months (P=0.01), a 0.70 mmHg increase in SBP from 9 to 15 months (p=0.046) and a 1.13 mmHg increase of SBP from 15 to 21 months (p=0.001), adjusted for the above covariates. The association with pulse pressure was similar. This study suggests that serum phosphate and its change over time are strong independent predictors of systolic and pulse blood pressure in hemodialysis patients. Rigorous control of serum phosphate levels in hemodialysis patients may help to optimize blood pressure and minimize its associated morbidity.

DISTRIBUTION AND ELIMINATION OF ^{45}CA AFTER ORAL ADMINISTRATION OF A CALCIMIMETIC IN CYNOMOLGUS MONKEYS IN THE PRESENCE OR ABSENCE OF CALCIUM LOADING. Charles Henley, Edward Shatzen, Fred Lott, David Martin. Metabolic Disorders, Amgen Inc, Thousand Oaks, CA

Soft-tissue calcification has been associated with disordered serum bone mineral levels in dialysis patients (pts). Previous studies have shown that the calcimimetics can reduce serum parathyroid hormone (PTH), calcium (Ca), phosphorus (P) and Ca x P, but pts may receive supplemental Ca (Ca loading), often as Ca-based phosphate binders. This study examined serum Ca disposition in animals treated with the calcimimetic AMG 641 in the presence or absence of Ca loading. Male cynomolgus monkeys were treated for 6 weeks with oral AMG 641 or vehicle with (n=4) or without (n=4) Ca acetate (100 mg elemental Ca po BID starting on day 37). $^{45}CaCl_2$ (50 μCi/kg) delivered in 1 mg/ml cold $CaCl_2$ diacetate (to minimize loss of ^{45}Ca) was given on days 15, 30, and 43, after which blood, urine, and fecal radioactivity was determined. Tissue radioactivity, determined 24 hrs after the terminal dose (day 43) was highest in bones (L3 vertebra [L3 vert] and femur) (Table, mean [SD]). Urine Ca increased in Ca-supplemented animals. The addition of cold $CaCl_2$ had a PTH lowering effect.

Tx Group	Serum Ca, mg/dL	Urine Ca, mg/dL	Radioactivity (ng equivalents $CaCl_2$/g)			
			L3 vert	Femur	Aorta	Kidney
Vehicle alone	10.2 (0.5)	42.3 (21.5)	1590 (1040)	1850 (720)	35.8 (14.2)	25.1 (10.4)
AMG 641 alone	8.9 (0.13)[a]	36.0 (25.1)	1660 (578)	2040 (582)	53.4 (16.3)	36.3 (8.1)
Vehicle + Ca	10.4 (0.5)	98.5 (46.0)[a]	1330 (228)	1630 (584)	30.6 (4.1)	24.5 (6.6)
AMG 641 + Ca	8.92 (0.75)[b]	81.9 (12.7)[c]	1940 (178)	2020 (782)	36.9 (11.6)	26.9 (6.4)

[a]$P<0.05$ vs vehicle, [b]$P<0.01$ vs vehicle + Ca, [c]$P<0.05$ vs AMG 641.

These data suggest that in normal animals, calcimimetic treatment with supplemental Ca intake will not promote accumulation of Ca in soft tissues, but instead may promote deposition into bone.

VITAMIN D DEFICIENCY IN DIALYSIS PATIENTS NOT ON VITAMIN D ANALOG THERAPY

Takashi Hato and James Ireland, University of Hawaii John A. Burns School of Medicine Department of Internal Medicine Division of Nephrology Honolulu, Hawaii, USA

Vitamin D analog therapy has become standard therapy for hemodialysis (HD) patients and is often titrated based on parathyroid hormone levels (PTH). Concern for adynamic bone disease has limited the use of vitamin D analogs in our practice when PTH levels are low. Because hypovitaminosis D may have an impact on mortality, we sought to determine the levels of 25 and 1,25 vitamin D in HD patients not on analog therapy.

We reviewed HD charts in one dialysis center for all patients from our four-nephrologist practice. Two groups were identified, those receiving and those not receiving vitamin D analog therapy.

We reviewed 72 charts and found 11 patients not on vitamin D analog therapy. Of those 11 patients, 10 were 1,25 vitamin D deficient with a median vitamin D level of 8.5 ng/ml (range 4-13) and a median PTH level of 68 pg/ml (range 5.2-175). Two patients were also found to have 25 vitamin D deficiency.

In our practice, 15% of our HD patients at one unit were not receiving a vitamin D analog, yet 91% were deficient in 1, 25 vitamin D and 18% were deficient in 25 vitamin D despite living in sunny Hawaii. Emerging mortality data for vitamin D deficiency will have to be balanced with the risk of adynamic bone disease in prescribing vitamin D analogs in HD patients with normal or low PTH levels.

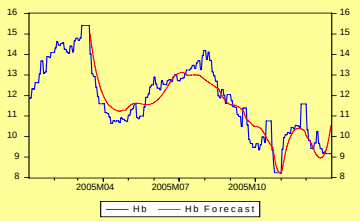
A TIME SERIES MODEL FOR HEMOGLOBIN RESPONSE IN DIALYSIS PATIENTS ON ERYTHROPOIETIN (EPO)

A K Gupta, Michigan State Univ., East Lansing, MI, USA
Anatole Besarab, Henry Ford Hospital, Detroit, MI, USA

The response of Hemoglobin (Hb) to EPO over time is complex. The influence of the lag needed to mature cells in the bone marrow and the impact of red cell survival lead to random variability and cycling. We attempted to study this using Time Series. The purpose of the analysis was to foster an understanding of the erythrocyte dynamics and to provide clinicians with better EPO dosing strategies.

Data including Hb (measured bimonthly) and EPO dosed 3 times/ week were abstracted from the Electronic Medical Record. Individual Time Series of Hb and EPO (first order autoregressive processes) and their cross-correlelogram functions (CCF) were plotted using STATA v.8.0. The relationship and the lag between the two series were studied. Finally, a polynomial distributed lag model was fitted to the data using E-views v.5.0. Dynamic forecasts were obtained. The forecasted Hb values were plotted against the observed Hb values.

The "sine wave" pattern of the CCFs provided clear indication of cycling. The CCF attained maximal values at variable lag periods (Range: 4 - 14wks.; mean ± SD, 8.5 ± 2.9, n= 30). The lagged EPO series followed the Hb series closely. An illustrative example with a lag period of 6 weeks is shown.



Clearly, multiple dose changes preclude attainment of a steady state Hb level. The mean lag of 60 days closely approximates the RBC survival in hemodialysis patients.

We conclude that Time Series models can be a useful tool for modeling and predicting the Hb response of a patient to EPO. While dosing EPO, one should attempt to minimize the number of dose changes. Future refinements of the model will include other determinants of EPO responsiveness such as iron stores and iron availability, demographic factors, and intercurrent events.

PERMANENT HEMODIALYSIS ACCESS IN A SUBURBAN END STAGE RENAL DISEASE POPULATION.

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Recent clinical practice guidelines recommend the creation of an arteriovenous access (AVF or AVG) before the start of chronic hemodialysis (HD). Permanent AV access prevents the complications associated with hemodialysis catheters. We report on the factors associated with timely creation of AV access in a suburban incident dialysis population.

All patients initiated on chronic HD between January 1, 2005 and December 31, 2005 in a suburban nephrology practice were included. Patients who initiated HD with a permanent AV access were compared with those who started HD with catheters.

We identified 122 patients (males 55, females 67), average age 66+_16.13 years, 70(57.4%) were whites, 42(34.4%)) blacks and 10(8.2%) Hispanics. Diabetic nephropathy was the most common cause of end-stage renal disease (43.4%).Forty three patients (35.2%) initiated dialysis with permanent AV access and seventy nine (64.8%) with a HD catheter.

We found no differences between the two groups with respect to age (68.3 vs.64.8 years, p=0.25) gender (Males 44.1% females 45.5%, p=0.88), race (60.5%whiteVs55.7%, p=0.21), etiology (51.25% diabetics Vs39.2%p=0.20), average Hemoglobin> 11g/dl prior to initiation of dialysis (48.8%Vs41.8%, p=0.45) and presence of commercial health insurance (67.44%Vs62.05%, p=0.55)

Patients with a permanent AV access were much more likely to have been referred to a nephrologist greater than 6 months prior to the initiation of HD (97.7% vs. 39.2% p<0.0001) and to have received erythropoietin therapy prior to the initiation of HD (74.4%vs.26.2%).In addition these patients were more likely to initiate dialysis in a non acute care setting (86%Vs62% p=0.005).

We conclude that in our dialysis cohort the single most important factor associated with timely creation of a permanent AV access was early referral to a CKD clinic, at least 6 months prior to the initiation of HD. 97% of patients who were enrolled in a CKD clinic 6 months prior to the initiation of HD began therapy with a permanent AV access.

THE FREQUENT HEMODIALYSIS NETWORK RANDOMIZED TRIAL OF HOME NOCTURNAL HEMODIALYSIS: CHANGE OF TRIAL DESIGN

Frequent Hemodialysis Network (FHN) Trial Group. NIDDK, NIH, Bethesda, MD, USA

The Frequent Hemodialysis Network (FHN), supported by NIH and CMS, has been conducting a randomized trial of home nocturnal HD (NHD) in 10 centers in the US and Canada. The initial trial design, with a control arm of 3 days/week in-center HD was changed 4 months after starting due to poor recruitment using the original trial design; few patients were willing to accept a 50% chance of being randomized to an in-center HD modality. In the revised design, both arms of the study will be done at home: 250 pts. with ESRD will be randomized 1:1 over a 26-month period to receive home NHD (6 nights/week, $\geq$6 hours per session, target standard or weekly Kt/V [stdKt/V] $\geq$ 4.0/week), or home conventional HD (3 days/week, $\geq$2.5 hrs/session, target stdKt/V approx. 2.2, eKt/V $\geq$ 1.1/session) for 12 months. All patients will undergo a 1-2 mo. training period prior to randomization.

The first yr. (beginning January 2007) has been designated as a Vanguard Phase, during which feasibility of randomization, ability to train patients, and adherence will be evaluated. If pre-defined recruitment and adherence benchmarks are met, the trial will continue to enroll patients for an additional 14 months. Two co-primary outcomes have been specified: i) the composite of mortality with the 12 mo. change in left ventricular mass index (LVMI) by magnetic resonance imaging, and ii) the composite of mortality with 12 mo. change in the SF-36 RAND Physical Health Composite (PHC). The 7 main secondary outcomes are: 1) change in LVMI, 2) change in PHC, 3) change in Beck Depression Inventory score, 4) change in Trail Making Test B score, 5) change in pre-HD serum albumin, 6) change in pre-HD serum phosphate, and 7) rate of non-access hospitalization or death. Changes in blood pressure and ESA requirements will also be assessed. Data will be obtained on the cost of delivering home HD, and cost-effectiveness of home NHD will be estimated mainly from the insurer's perspective. Conclusion: Our initial experience suggests that a randomized trial of home vs. in-center dialysis therapy is difficult to achieve in practice among patients willing to do home dialysis.

PROGRESS OF THE FREQUENT HEMODIALYSIS NETWORK RANDOMIZED TRIAL OF IN-CENTER DAILY HEMODIALYSIS

Frequent Hemodialysis Network (FHN) Trial Group. NIDDK, NIH, Bethesda, MD, USA

Purpose: The Frequent Hemodialysis Network (FHN), supported by NIH and Centers for Medicare & Medicaid Services, is conducting a randomized trial of daily versus conventional HD in 11 centers in the US/Canada. 250 patients with ESRD will be randomized 1:1 over a 26-month period to receive in-center daily HD (6 days per week, 1.5 to 2.75 hrs/session, target eKt/V 0.9), or conventional HD (3 days per week, $\geq$ 2.5 hrs/session, target eKt/V$\geq$1.1) for 12 months. Because no large-scale randomized trials of daily HD have been previously conducted, the first year (beginning June 2006) was designated a Vanguard Phase, during which feasibility of randomization and ability to deliver the interventions will be evaluated. If pre-defined recruitment and adherence benchmarks are attained, the trial will proceed to determine the effects of daily HD on several parameters. Two co-primary outcomes have been specified: i) the composite of mortality with the 12 month change in left ventricular mass index (LVMI) by magnetic resonance imaging, and ii) the composite of mortality with 12 month change in the SF-36 RAND Physical Health Composite (PHC). The 7 main secondary outcomes are: 1) change in LVMI, 2) change in PHC, 3) change in Beck Depression Inventory score, 4) change in Trail Making Test B score, 5) change in pre-HD serum albumin, 6) change in pre-HD serum phosphate, and 7) rate of non-access hospitalization or death. Changes in blood pressure and erythropoeisis will also be assessed. Safety will be evaluated, with emphasis on vascular access complications, iron losses, and treatment burden. Finally, data will be obtained on the incremental cost of delivering daily HD over conventional HD.

Results: In the first 6 months, 117 (132% of goal) patients have been enrolled into baseline, 24 (21%) excluded before randomization, 28 still in baseline, and 65 randomized (116% of goal). Hence, recruitment has been above target. Adherence to the assigned dialysis frequencies in the most recent month has been excellent over all: 97% and 85% in the 3 and 6xweek arms, respectively.

Conclusion: The trial is on target for meeting its goals.

ADVANCE: THE EFFECT OF CINACALCET + LOW-DOSE VITAMIN D ON VASCULAR CALCIFICATION IN HEMODIALYSIS PATIENTS – METHODS

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Vascular calcification (VC) in hemodialysis (HD) patients has been associated with elevated serum calcium (Ca) and phosphorus (P) concentrations. Preclinical evidence suggests that the calcimimetic cinacalcet does not induce VC and attenuates vitamin D-associated VC. Clinical studies have shown that cinacalcet + low-dose vitamin D improves control of parathyroid hormone (PTH), Ca, P, and Ca x P in HD patients. However, the effect of cinacalcet on VC has not been examined. In this multi-center, randomized, open-label trial, subjects (projected total n=330) with iPTH ≥300 pg/mL (or 150-300 pg/mL with Ca x P >50 mg^2/dL^2 and on vitamin D [to capture subjects with secondary HPT with controlled PTH]), a corrected serum Ca ≥8.4 mg/dL, and a coronary artery calcification (CAC) score of ≥30 will be randomly assigned to receive cinacalcet + low-dose vitamin D or flexible vitamin D without cinacalcet for 20-week dose-titration and 32-week follow-up phases. Cinacalcet will be started at 30 mg/day and titrated to 60, 90, 120, and 180 mg/day, as appropriate based on PTH concentrations. In the group not receiving cinacalcet, vitamin D (initiated at a maximum of 2 mcg paricalcitol or equivalent per dialysis session) will be titrated according to clinical practice guidelines. The primary study endpoint is the percent change from baseline to week 52 in CAC.

IMPROVING INTERDIALYTIC WEIGHT GAIN. Noelle Fein, Laura Lindsey, Fresenius Medical Care, Gresham, OR, USA.

Chronic hemodialysis patients often exceed target interdialytic weight gain (IDWG) putting them at risk for hypertension, cardiac events, and mortality. While individual counseling is routinely performed to educate patients on dietary sodium and fluid restrictions, group education with the intent to lower IDWG had not been done at our unit. In 2006, a CQI project was implemented with a goal to improve IDWG to $\leq$ 3 kg..

The intervention consisted of several educational bulletin boards, crossword puzzles, and simple fluid diaries. The goals of the bulletin boards were to address the risks of high IDWG and myths regarding fluid and sodium intake, provide information on reducing sodium and fluid intake, and show visual displays of daily allotted fluid intake.

Mean IDWG was recorded for each patient in the month proceeding, during, and after the intervention. The percentage of treatments meeting the goal of $\leq$ 3 kg. was also tracked. The paired t-test was used to determine if the mean IDWG differed for each patient from baseline. Changes in alb were also analyzed using the paired t-test as nutritional status may impact IDWG.

There was no significant change in mean IDWG from baseline during the intervention ($p = 0.22$) or in the month following the intervention ($p = 0.25$). The total percentage of pts with mean IDWG $\leq$ 3 kg. before, during, and after the study was 61%, 61%, and 55% respectively. The percentage of pts meeting the goal of $\leq$ 3 kg. for at least 75% of treatments before, during, and after the study was 42%, 39%, and 39% respectively. Albumin levels did not significantly change.

Unfortunately IDWG did not improve following the intervention. Perhaps offering nominal prizes to patients meeting weight gain goals or designing educational games would help motivate patients to decrease IDWG. The intervention focused primarily on the preparation and action stages of change. Several health behavior change studies that apply the transtheoretical model have found that the majority of individuals are in the precontemplation stage of change. Identifying patients in the different stages of change and developing interventions that target these individuals may improve outcomes.

A RANDOMIZED, DOUBLE-BLIND, CROSS-OVER DESIGN STUDY OF SEVELAMER HYDROCHLORIDE (SH, RENAGEL®) AND SEVELAMER CARBONATE (SC) IN CHRONIC KIDNEY DISEASE PATIENTS ON HEMODIALYSIS

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Background: SC is a new phosphate binder with the same polymeric structure as SH in which carbonate replaces chloride as the counterion. SC is calcium- and metal-free. The purpose of the study was to investigate the effects of SC and SH on the control of serum P in hemodialysis patients.

Methods: This was a double-blind, randomized, cross-over study. Following a 5 wk, SH run-in period, 79 hemodialysis patients were assigned randomly (1:1) to either SC for 8 wks followed by SH for 8 wks, or SH for 8 weeks followed by SC for 8 weeks. A 2-week washout followed the active treatment phase. The starting dose was individualized for each patient based on the most recently prescribed daily dose during the run-in period. A stable dose of cinacalcet and vitamin D were maintained, unless changes were needed for safety reasons.

Results: The mean actual daily dose for both SC and SH was 6.0 ± 2.8 g/day. No patients changed their sevelamer daily dose during randomized treatment. The mean serum P was 4.6 ± 0.9 mg/dL during SC treatment and 4.7 ± 0.9 mg/dL during SH treatment. The geometric least square mean ratio (SC/SH) was 0.99 with a 90% CI of 0.95-1.03, indicating that SC and SH are equivalent in controlling serum P. There were no clinically significant differences between treatment groups in lipid profiles. SC and SH have a similar safety and tolerability profile.

Conclusion: In hemodialysis patients, SC and SH were equivalent in controlling serum phosphorus.

HEMODIALYSIS FOR HYPERAMMONEMIA ASSOCIATED WITH ORNITHINE TRANSCARBOMYLASE DEFICIENCY

Jacob Collen, Jonathan Koff, Kevin Abbott, Nealanjon Das

INTRODUCTION: Acute hyperammonemia requires prompt recognition and rapid reduction of serum ammonia to prevent devastating sequelae of cerebral edema and neuronal death. Etiologies of hyperammonemia due to hepatic failure, drugs, and defects of urea cycle enzymes should be investigated. Ornithine transcarbomylase (OTC) deficiency is a well-known but uncommon inherited cause of hyperammonemia. Late-onset or partial deficiency goes unrecognized in adults until presenting dramatically with encephalopathy or coma. Treatment to prevent adverse neurologic outcomes includes immediate removal of serum ammonia with dialysis, and adjunctive administration of lactulose, sodium phenylacetate and benzoate, and arginine to address the ammonia production resulting from enzymatic deficiency.

CASE REPORT: A 34-year-old male presented with nausea, vomiting, weight loss, intolerance of meat and protein supplements, and delirium leading to stupor and coma. CBC, renal and hepatic function, and CSF analyses were unremarkable. Seizures developed and CT scans showed progressive cerebral edema. Initial serum ammonia levels of 125mg/dL rose to 912mg/dL. Immediate initiation of hemodialysis upon presentation to our tertiary care center reduced ammonia levels to 21mg/dL after 26 hours of dialysis. Dialysis was redosed intermittently and successfully reduced interdialytic elevations of ammonia above 125mg/dL. Intravenous arginine, sodium phenylacetate, and sodium benzoate were administered. Central diabetes insipidus with polyuria and hypernatremia developed due to cerebral edema and pituitary stalk compression. Despite aggressive treatment measures, the patient suffered brain death. Elevated urinary orotic acid levels of 609 mmol confirmed the diagnosis of late-onset ornithine transcarbomylase deficiency.

CONCLUSIONS: This case highlights the importance of considering inherited metabolic disorders in hyperammonemic patients with encephalopathy who present atypically and with normal hepatic function. Early recognition and management, to include acute hemodialysis while awaiting diagnosis of enzymatic deficiencies of the urea cycle, is crucial in preventing lasting neurologic damage.

SUSTAINED LOW EFFIENCY DIALYSIS (SLED) WITH REGIONAL CITRATE ANTICOAGULATION (RCA) IS WITHOUT METABOLIC COMPLICATIONS, BUT AT THE COST OF INCREASED CALCIUM DOSE.

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Patients that may benefit from SLED therapy, particularly in the ICU, are at risk for bleeding. Thus, anticoagulation strategies that are safe and simple to use would be of great benefit. We propose that modifying pre-existing RCA protocols to our increased SLED dose will provide safe and effective anticoagulation.

We used Fresenius® 2008H or K machine for 8hr SLED treatments at a blood flow (Qb) rate of 250cc/min and dialysate flow (Qd) rate of 300cc/min. The circuit was anticoagulated with a 4% Sodium Citrate solution provided by Baxter© (Citrate 136 mmol/L and Sodium 408 mmol/L) and a Calcium Chloride ($CaCl_2$) infusion. Standard Bicarbonate (37mEq/L) dialysate without Calcium was used. Every 2 hrs a BMP, ionized circuit and ionized patient Ca was monitored.

There were 7 patients and 36 treatments providing 245 hrs of open circuit time. The protocol was titrated to maintain ionized Ca of 4.0-4.8 mg/dl with initial Citrate infusion ~33.9 mmol/hr. After 8hrs, the citrate infusion was 33.5 mmol/hr ($p=0.024$). Citrate infusion maintained the circuit ionized Ca levels between 0.82-0.84 mg/dl. The Ca ion infusion baseline was 38.3 mmol/hr, but increased by 8hrs to 43.3 mmol/hr ($p<0.05$). Despite increasing Ca infusions, the patients ionized Ca decreased from 4.7 mg/dl to 4.2 mg/dl ($p<0.05$). Sodium was unchanged at 139.5 mEq/L ($p=0.52$). The bicarbonate increased from 25.9 to 29.7 mmol/L ($p<0.05$). Total Calcium baseline was 9.17 mg/dl and final 8.73 mg/dl ($p=0.37$).

RCA can be performed on our 8hr SLED therapy without metabolic complications. The infusions of 4% Sodium Citrate and $CaCl_2$ did provide safe and effective anticoagulation, although at the cost of increasing Ca infusion due to removal of Ca-Citrate complex with our increased SLED dialysis dose.

ASSESSING THE USE OF THE CALCIMIMETIC CINACALCET WITH LOW DOSE VITAMIN D VERSUS ESCALATING DOSES OF VITAMIN D ALONE IN THE TREATMENT OF SECONDARY HYPERPARATHYROIDISM (HPT)—THE ACHIEVE STUDY

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The calcimimetic cinacalcet effectively lowers parathyroid hormone (PTH) and improves mineral metabolism in hemodialysis (HD) patients with secondary HPT, independent of vitamin D (vit D) use. The ACHIEVE study compared the treatment regimens of cinacalcet plus low-dose vit D (paricalcitol/doxercalciferol) to escalating doses of vit D without cinacalcet and the relative efficacy in achieving simultaneous control of iPTH and Ca x P (as described by KDOQI™ goals) in HD subjects with secondary HPT. Mean iPTH increased while Ca x P decreased after a 3 wk vit D washout period. (Table 1)

Mean (SD)	Pre-Washout (n =173)	Post-Washout (n =173)
iPTH, pg/mL	440.6 (157.3)	651.5 (234.8)
Ca, mg/dL	9.9 (0.7)	9.6 (0.6)
P, mg/dL	5.7 (1.6)	5.3 (1.7)
Ca x P, mg^2/dL^2	56.6 (15.9)	50.8 (15.7)

After washout, subjects were randomly assigned to cinacalcet plus low dose vit D or vit D alone. Key mean baseline variables were similar between treatment groups. (Table 2)

	cinacalcet +vit D (n=87)	vit D only (n=86)
iPTH, pg/mL	643.1 (231.7)	660.0 (239.0)
Ca, mg/dL	9.6 (0.6)	9.7 (0.5)
P, mg/dL	5.3 (1.7)	5.3 (1.7)
Ca x P, mg^2/dL^2	50.2 (15.1)	51.4 (16.4)
P-binder use	98 %	98 %
Pre-washout vit D	99 %	99 %

Vit D washout increased PTH, and lowered Ca x P and serum P levels. This suggests that a treatment approach suppressing PTH while reducing the need for large doses of vit D may be optimal for the management of secondary HPT.

REASONS FOR HEMODIALYSIS CATHETER USE & ITS COMPLICATIONS: PATIENT AND COORDINATOR PERSPECTIVES

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Catheters (CVC) for hemodialysis access are associated with significant morbidity and mortality, yet CVC use continues to be high. This study aims to 1) determine the reasons why patients use CVC from 2 perspectives i) the patient and ii) the vascular access coordinator (VAC) ; and 2) compare these perspectives. Additionally, the complication of central venous stenosis (CS) may limit the creation of a future permanent access. Therefore, the prevalence and impact of CS is examined. 165 patients from a large, tertiary centre and their VAC were independently surveyed using a standardized questionnaire on CVC use. An interventional radiologist reviewed all venograms in patients who had at least one CVC exchange to determine the presence of CS. The results are summarized in the following table:

MAIN REASONS FOR CVC USE	PATIENT (% of total)	VAC (% of total)	BOTH (% of total)
Needle phobia	40 (24%)	0	0
Prior failed fistula/graft, does not want or unable to go on to peritoneal dialysis, does not want other surgery	29 (18%)	5 (3.0%)	3 (1.8%)
Cosmetic appearance of fistula/graft	24 (15%)	0	0
Patient Preference	1 (<1%)	57 (35%)	2 (1.2%)

Table 1: Reasons for CVC use, as cited by patients, VAC, or both (not all data shown).

There was<15% agreement in views amongst patients and the VAC regarding the reason for CVC use. Primary reasons were needle phobia and surgical fatigue (patients' views) and patient preference (VAC view). <5% were waiting for new access creation or maturation or had a medical contradiction to access creation. 40% had CS and may limit future access creation. Understanding specific patient concerns, and greater patient education of the risk of CVC use, its complications and consequences is required to reduce CVC use and promote optimal access care.

PROTECTIVE ROLE OF AT_1 BLOCKADE IN RENAL TISSUE IN UNINEPHRECTOMIZED SHR & WKY RATS.

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After local injury angiotensin II produces proinflammatory effects and potential fibrosis in various tissues including kidney. Uninephrectomized (UNX) spontaneously hypertensive rats (UNX-SHR) develop earlier glomerular hyperfiltration and interstitial damage of the remnant kidney. Therefore, UNX-SHR is a useful animal model to investigate mechanisms involved in the progression of hypertensive renal disease. Our aim in the present study was to evaluate whether AT1 blockade may reduce inflammatory response in renal tissue by controlling Plasminogen activator inhibitor-1(PAI-1) and Collagen type III (Col-III) in UNX-SHR. Male SHR and Wistar Kyoto (WKY) underwent uninephrectomy at 10 weeks old and were subsequently assigned to the following schedule during six months: [G1] UNX-SHR; [G2] UNX-WKY; [G3] UNX-SHR with valsartan 50 mg/kg/day. [G4] UNX-WKY with valsartan 50 mg/kg/day. Creatinine clearance (Crcl), proteinuria and systolic blood pressure, were evaluated. PAI-1, alfa-smooth muscle actin (a-SMA) and Col-III were assessed by immunohistochemistry. Results at the end of the experiment:

Crcl (µl/min/g BW): G1=1.2 ± 0.1*, G2= 2.9 ± 0.1; G3= 2.6 ± 0.3, G4=3.9 ± 0.2**. Proteinuria (mg/day): G1= 253 ± 39*, G2= 63 ± 10; G3= 67 ± 9, G4= 15 ± 7**. SBP (mmHg): G1= 218* ± 17, G2= 154 ± 7; G3= 147 ± 8, G4= 121 ± 3**. PAI-1 (%/area): G1= 20.7±3.1*, G2= 8.7±2.4; G3= 13.9±1.8***, G4= 5.1±1.4**. a-SMA (%/area): G1= 26.7±3.5*, G2= 13.8±2.4; G3= 16.5±2.1, G4= 5.7±2.9**. Col III (%/area): G1= 18.8±3.6*, G2= 8.9±1.7; G3= 9.7±2.2, G4= 2.3±1.1**. ($p<.01$* vs. all Gs; $p<.01$** vs. G2 & G3; $p< 0.01$*** vs. G2). Conclusions: AT1 blockade reduces PAI-1, and aSMA immunostaining together with a substantial control in Col-III deposition in renal tissue not only of SHR-UNX but also WKY-UNX. These results reinforce the important role in modulating angiotensin II actions especially in hypertensive renal disease.

PREVELENCE OF WHITE COAT EFFECT IN HEMODIALYSIS PATIENTS AS DETERMINED BY A STANDARDISED AUTOMATED BLOOD PRESSURE MEASUREMENT.

Manish M Sood, Marisa Battistella, Charmaine E. Lok, Robert Richardson. Toronto, Ontario, Canada. M5G2C4.

Accurate measurement of blood pressure (BP) in hemodialysis patients is crucial to their BP management. Blood pressure measurements in the hemodialysis unit are often inaccurate. The white coat effect in hemodialysis patients is the transient rise of blood pressure in the hemodialysis unit. The purpose of this study was to prospectively determine the prevalence of “white coat effect” in hemodialysis patients by comparing predialysis BP measurements obtained by standard hemodialysis methods (STD BP) with those obtained using an ideal BpTRU[TM] measurement.

Pre-dialysis STD BPs were obtained while the patient was in their dialysis chair using the automated machine as per standard practice. On a subsequent day, the same patient’s BP was measured under “ideal conditions” using BpTRU measurements. The BpTRU (VSM MedTech Ltd, Vancouver, Canada) measurement is a standardized, validated method of measuring blood pressure. Seventy-one patients were screened and identified using STD BP as hypertensive according to NKDOQI guideline definitions (>140/90) with an average value of 161/89 mmHg. In contrast using the BpTRU, the average blood pressure was 134/76 mmHg. Thirty-two out of 71 patients (45%) previously labeled as hypertensive had normal blood pressure measurements with average reductions of 27 mmHg (systolic) and 13 mmHg (diastolic). Among those with the white coat effect, the average reductions in systolic and diastolic blood pressures were 38 mmHg (systolic) and 16 mm Hg (diastolic) when comparing STD BP to BpTRU measurements.

In conclusion, the BpTRU method identified a 45 % incidence of white coat effect in a prospective cohort of chronic hemodialysis patients. This may have implications with respect to diagnosis and treatment of hypertension in our dialysis population. Further studies to determine the reasons for this white coat effect and correlations of STD BP and BpTRU measurements with 24 hour BP monitoring are underway.

THE RELATIONSHIP BETWEEN BLOOD PRESSURE, OBESITY, ENDOTHELIN-1 AND PLASMA LIPIDS IN A GULF ARAB POPULATION

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This study sought to evaluate the relationship between blood pressure, obesity, dyslipidemia, fasting plasma levels of glucose (Glu), insulin (Ins) and endothelin-1 (ET-1) in United Arab Emirates (UAE) nationals.

The study was conducted between the period of April 2002 to October 2005 in Al-Ain, United Arab Emirates. Plasma levels of lipids, lipoproteins, glucose, insulin and endothelin-1 (ET-1) were measured after overnight fasting in 215 UAE nationals, including 93 with untreated hypertension.

In hypertensives, the levels of ET-1, non-esterified fatty acids (NEFA), triacylglycerols (TG), glucose (Glu) and insulin (Ins) were increased, but only significantly ($p<0.001$) for the first two parameters. High-density lipoprotein- (HDL) total cholesterol was significantly ($p<0.001$) decreased in hypertensives, but total and low-density lipoprotein- (LDL) cholesterol levels were unchanged. Taken as a single group, both systolic and diastolic blood pressures were significantly ($p<0.01$) correlated with plasma levels of NEFA, ET-1, and less significantly ($p<0.05$) with Ins and correlated inversely ($p<0.01$) with HDL- cholesterol. Plasma levels of NEFA and HDL-cholesterol were significantly ($r=0.33$; $p<0.01$) correlated directly and inversely ($r=-0.25$; $p<0.01$) respectively with ET-1 levels and inversely ($r=-0.16$; $p<0.05$) with each other. Partial correlation analysis showed that the correlations between blood pressure and ET-1 levels and HDL, but not NEFA, were independent of a range of other variables. Similarly, the correlations between ET-1 levels and HDL and NEFA were independent of the other variables, but not so the inverse correlation between HDL and NEFA.

In conclusion, the results point to the importance of both raised ET-1 and dyslipidaemia in hypertension in the UAE national population and suggest an association between ET-1 and lipoprotein metabolism in the vascular endothelium.

HYPERHOMOCYSTEINAEMIA AND TYPE IV HYPERTRIGLYCERIDAEMIA ARE COMMON CARDIOVASCULAR RISK FACTORS IN HYPERTENSIVES

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This study was initiated to quantify various risk factors for hypertension in a heterogeneous population.

A random sample of 170 hypertensive subjects (mean age ± SEM; 46.7 ± 0.6 yrs) and 170 healthy non-obese normotensive subjects (46.1 ± 0.6 yrs) were closely matched for age, gender and ethnicity. Fasting plasma samples were used to measure endothelin-1 (ET-1), nitric oxide (NO), homocysteine (Hcy), and insulin by ELISA methods. Lipids, lipoproteins, blood urea nitrogen (BUN), creatinine, and glucose were measured by colorimetric methods.

Hypertensives had significantly ($p<0.01$) higher levels of Hcy, NO, ET-1, insulin very low-density lipoprotein (VLDL) and triglycerides (TG) and lower levels of total cholesterol (TC) and low-density lipoprotein-cholesterol (LDL–C) as compared to normotensives.

Moreover, Hcy correlated postively with Age, SBP, DBP, NO, BUN, creatinine, TG, VLDL, and inversely with High Density Lipoprotein Cholesterol (HDL-C) and Body Mass Index (BMI). Also, NO positively correlated with SBP, BUN, creatinine, and inversely with TC, HDL-C, and LDL, no significant correlations were observed for ET-1.

In this study, hyperhomocysteinaemia is associated with hypertension, increased age, SBP, pulse, BUN and creatinine and may thus be a valuable marker in the etiology of hypertension particularly among the older population. The abnormally elevated levels of TG and VLDL in association with normal TC levels seem to indicate typical characteristics of Type IV hyper-triglyceridaemia among hypertensives and may constitute a significant risk factor for vascular complications.

GENETIC VARIATION WITHIN ADRENERGIC PATHWAYS DETERMINES *IN VIVO* EFFECTS OF PRESYNAPTIC STIMULATION IN HUMANS. Maple M Fung, Carie Nguyen, Parag Mehtani, Rany M. Salem, Brandon Perez, Brenda Thomas, Daniel T. O'Connor. University of California at San Diego, La Jolla, CA, USA.

Catecholamines play a dominant role in minute-to-minute blood pressure regulation. We hypothesized that inter-individual variation in catecholaminergic responses are in part genetic and may contribute to the complex heritability of hypertension.

To evaluate such responses in the absence of systemic (baroreceptor) counter-regulation, we locally infused graded concentrations of tyramine, an indirect presynaptic norepinephrine releaser, into dorsal hand veins of 49 healthy, normotensive adults of both sexes and 5 ethnicities. The vascular responses were coupled to common (minor allele frequency >10%) single nucleotide polymorphisms (SNPs) at adrenergic target loci within presynaptic catecholamine pathways.

Vasoconstriction progressed from baseline (0%) to 44% (of vein diameter) with increasing concentrations of tyramine (0.129 - 25.8 mmol/L) (repeated measures ANOVA, $P<0.01$). Family history of hypertension (FH-htn) also predicted tyramine response ($P<0.05$).

Because of racial variation in SNP frequencies, ethnicity was factored as a covariate. Significant vasoconstriction associations were noted at 2 SNPs encoding proteins catalytic in catecholamine secretory vesicle formation, chromogranin A (promoter, G-462-A) ($P<0.01$) and chromogranin B (exon 4, Glu348Glu; $P<0.05$). SNPs for cytochrome b-561, an electron shuttle for catecholamine synthesis (intron 1,C+602G, $P<0.01$) and subunit beta of vacuolar ATPase, which acidifies the vesicle, (exon 1, Ile30Thr, $P<0.05$) were also significant predictors. Association was not noted for the enzymes flavin monooxygenase 3 (E158K), tyrosine hydroxylase (promoter C-824T), and dopamine beta-hydroxylase (promoter C1021T). Pathway analysis indicated a global effect of genetic variation on the pressor response ($P=0.025$).

In conclusion, locally infused tyramine produced a dose-dependent pressor response, which was predicted by FH-htn and by multiple SNPs that encode for the biosynthesis, storage, and release of catecholamines. Such variants may influence the complex heritability of adrenergic responses and then in the predisposition to hypertension.

GENERALIZED VASOCONSTRICTION AND ACUTE HYPERTENSION PRODUCED BY THE CALCIMIMETIC, CINACALCET, IN UREMIC AND NORMAL RATS

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Cinacalcet (CIN) decreases serum PTH and Ca in ESRD patients with SHPT and also produces acute elevations in blood pressure (BP) in uremic rats. To test the hypothesis that CIN produces acute hypertension through vasoconstriction of multiple vascular beds, the regional hemodynamic effects of CIN were delineated in anesthetized rats and correlated to changes in BP and iCa^{2+}.

Male SD rats were subjected to 5/6 nephrectomy (NX) or no surgery (Normal); at 7-8 weeks uremia rats were instrumented to record BP, heart rate and regional blood flow (carotid, mesenteric, hindlimb). CIN (1, 3, 10 mg/kg; 30 min/dose) or VEH was infused over 90 min. Change from baseline in CIN *vs.* VEH was analyzed by repeated measures ANOVA, Dunnett's (*$p<0.05$).

In NX, CIN decreased iCa^{2+} from 1.22±0.02 mmol/L at baseline to 1.10±0.02*, 0.97±0.02* and 0.91±0.03* mmol/L and produced increases in BP (from 119±6 mmHg to 129±5, 142±4*, and 145±3* mmHg at the end of each infusion). At 1 mg/kg carotid (CVR) and mesenteric (MVR) vascular resistance increased to 16±6%* above baseline (VEH=3±2%) and 18±6*% above baseline (VEH= -1±2%), respectively. Hindlimb (HVR) vascular resistance trended upward to 13±8% above baseline (VEH = -2±2%). At 3 mg/kg increases in CVR (38±10%*), MVR (40±8%*) and HVR (39±14%*) were exacerbated; at 10 mg/kg values remained at or near these levels.

The effects of CIN on iCa^{2+}, BP and VR in Normal rats were similar to NX. Thus, at doses producing reductions in iCa^{2+} CIN acutely increases BP in uremic and non-uremic rats, responses that occur in parallel to vasoconstriction in vascular beds fed by the carotid, mesenteric, and hindlimb arteries.

HYPERTENSION PREVALENCE IN CHINATOWN CLINIC

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Prevalence of High Blood Pressure (HBP) among Asians at the Philadelphia Chinatown Clinic was determined by review of 1,322 charts. Pts with HBP were analyzed for systolic (S) BP, diastolic (D) BP, glucose, medications, ethnicity, gender, and years in US.

Of 1,322 subjects, 288 presented to clinic with HBP (21.8%). 14/288 had Diabetes (4.9%). 174 were Indonesian with av BP of 151/91 and 55 were Chinese with an av BP of 151/91. Initial BP in 110 males was 148/92 and in 155 females was 154/91. Av BP for subsequent visits was 139/88 for males and 139/86 for females. BP increased with years of U.S. residence: <2 yrs 148/90; 2-4 yrs 150/92; >4 yrs 157/96. Mean random serum glucose of 287 pts was 150 mg/dL and of Diabetics was 253 mg/dL. BP control was categorized into 4 groups: I. No improvement or worse, 43 (33%) mean BP 145/90 at 1st visit to 158/94 at last visit. II. Improvement but not JNC7 goal (BP<140/90), 34 (26%), 171/96 to 147/91, decrease in SBP 24 mmHg, DBP 5mmHg. III. Reached goal, but did not sustain goal, 15 (12%), 150/91 to 150/93. However, mean lowest BP of III was 122/78. IV. Reached goal and sustained, 38 (29%), 152/94 decreased to 124/81. Of 288 pts, 181 were not given drugs, 60 returned for follow up: 21 pts had no improvement, 11 patients had improvement but not goal, 3 patients reached goal but did not sustain the goal BP, and 25 reached and sustained goal BP. 70 of 107 pts given drugs returned for follow up: 18 showed no improvement, 23 pts had improvement but not goal BP, 12 patients reached goal but did not sustain the goal BP, and 13 patients reached and sustained BP goals. Drugs given: HCTZ 78, Enalapril 51, β Blocker 27 and Amlodipine 3. 158 of 288 were lost to follow up (55%).

Chinese and Indonesians showed no BP difference. Initial female BP 154/91 was greater than male BP 148/92. Subsequent female BP was similar to the male BP at 139/86 vs. 139/88. Increasing BP with years in US reveals westernization affects BP in Asians, corroborating studies of risk factors of country of destination, not country of origin. High drop out rate was noted and 30% met JNC7 requirements for HBP drug therapy. Asian pts given HBP drugs were more likely to return for follow up than pts not given HBP drugs.

PULMONARY HYPERTENSION (PH) IS PREVALENT IN PERITONEAL DIALYSIS (PD) PATIENTS (PTS) AS WELL AS HEMODIALYSIS (HD) PTS.

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We have reported that PH is highly prevalent and may affect outcome in hemodialysis pts. There is no information available in the literature regarding the prevalence or clinical characteristics of PH in PD pts. We collected the demographic characteristics, clinical profile, biochemical data, and echocardiographic findings (ECHO) of 151 HD and 36 PD pts who had an ECHO performed for any reason. PH, defined as pulmonary artery pressure (PAP) $\geq$30 mm Hg was found in 64% of HD and 58% of PD pts. HD pts with PH tended to be older than PD pts with PH (61 vs. 56 years, p=0.06), but there were no differences in race and gender. The prevalence of diabetes was significantly higher in PH pts on HD compared to PD (48% vs. 24%, p=0.04). Mean PAP was significantly higher in HD pts compared to PD pts (47±12 vs. 40±9.5 mm Hg, p=0.01). Cerebrovascular accident (CVA) was more common in PD compared to HD pts with PH, but there were no significant differences in peripheral vascular disease (PVD), congestive heart failure (CHF), coronary artery disease (CAD) or chronic obstructive pulmonary disease (COPD) between the HD and PD patients. The ECHO characteristics of PH pts, such as ejection fraction, left ventricular hypertrophy, diastolic dysfunction or right atrial dilatation were similar, but PD pts tended to have more mitral valve calcification compared to HD pts (29% of PD pts vs. 12% of HD pts, p=0.08). Serum albumin was significantly higher (3.74±.52 vs. 3.28±0.69 g/dL, p=0.001) and parathyroid hormone (PTH) was significantly lower (397±323 vs. 588±427 pg/L, p=0.04) in HD compared to PD pts. Demographic and clinical differences were more likely related to modality than to etiology of PH. In summary, PH is as highly prevalent in PD pts as HD pts.

“PD” PERITONEAL DIALYSIS OR PERSONAL DEDICATION

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Peritoneal Dialysis (PD) as a modality for renal replacement therapy (RRT) is clearly underutilized in USA despite various benefits, including possibly better early survival. The percentage of PD population amongst end stage renal disease (ESRD) patient population in Southern California Kaiser Permanente (SCPMG) is still very low. There are various factors for this.

We attempt here to explore the possibility and impact of training of individual nephrologists, their personal preference and enthusiasm regarding PD. We looked at the data from one Kaiser Hospital and reviewed the distribution of PD patients amongst all the nephrologists within the same group taking care of similar patient population. The percentage of PD starts for 2006 year amongst total dialysis startups (PD and HD) for each nephrologist was calculated. Wide variations amongst nephrologists regarding utilization of PD were noted, from as low as 0 % to as high as 52 %. This variation directly correlated with the training background of the nephrologists and hence their preferences.

We believe that utilization of PD can be significantly enhanced in a large group like SCPMG by enhancing the education, comfort level and enthusiasm regarding PD amongst individual nephrologists. Because of being one big group, targeting individual nephrologists for this purpose should be relatively easy. It can be seen that up to 52 % of new ESRD patients in USA can be initiated on PD.

Emphasis should be placed on nephrologists to put their PD (personal dedication) into their patients’ PD (peritoneal dialysis).

EFFICACY OF HEPATITIS-B VACCINATION IN PATIENTS MAINTAINED ON PERITONEAL DIALYSIS **Fakhar Ijaz, Umapati Hedge, Cynthia Newton, Michael Baggett, Irfan Sohail, Fatima Syed, Satyaki Banerjee, Muhammad G. Alam**

The CDC currently recommends routine HepB vaccination of all patients with ESRD. Patients with ESRD known to have poor response to HepB vaccination compared to the general population. In 2000, we initiated a vaccination protocol in patients undergoing peritoneal dialysis (PD). All the patients who were tested negative for HepB were given Engerix 40 mcg IM (deltoid) injections at 0, 1, 2, and 6 months. Forty-five patients received vaccination from 2000-2005 and have HepB surface antibody test results available. A person with a HepB surface antibody titer less than five was considered as a non-responder.

There were 69% male, 57.8% non-black, 84.4% on automated peritoneal dialysis (APD), and 49% had diabetes mellitus (DM).

	Responder	Non Responder	*P*-value
Age (yrs)	50.47	52.46	0.65
BMI	26.8	28.57	0.32
Time on dialysis (yr)	2.5	2.37	0.69
Residual Renal Function	0.69	0.6	0.67
Total Kt/V	2.25	2.19	0.78
Serum Albumin (gm/dl)	3.5	3.2	0.06
Serum Ferritin (ngm/ml)	394	298	0.31
Hemoglobin (gm/dl)	12.06	11.32	0.17

Vaccination response rates were high in females (8/14vs9/31) and blacks (10/19vs7/26) although results did not reach statistical significance because of a limited number of patients. Only 5/22 patients with DM responded compared to 12/22 non-diabetic patients (p= 0.03). Patients on APD had significantly poor response compare to patients on CAPD. In APD patients 11/38 compared to 6/7 CAPD patients responded to vaccination (p=0.004).

The seroconversion rate for patients with ESRD maintained on PD at our institution was documented to be 37.8%. This result is lower than the expected published rate of positive conversion of 49% to 72.7%. Patients on APD and with DM had extremely poor response to HepB vaccination.

AUTOMATED PERITONEAL DIALYSIS IS ASSOCIATED WITH POOR RESPONSE TO HEPATITIS-B VACCINATION

Fakhar Ijaz, Umapati Hedge, Cynthia Newton, Michael Baggett, Irfan Sohail, Fatima Syed, Satyaki Banerjee, Muhammad G. Alam

The CDC currently recommends routine hepatitis-B vaccination of all patients with ESRD. Patients on peritoneal dialysis have poor response to hepatitis-B vaccination. Previous studies have not described in detail the seroconversion rate in response to hepatitis B vaccination in patients with ESRD maintained on automated peritoneal dialysis (APD). In 2000, we initiated a vaccination protocol in patients undergoing peritoneal dialysis. All the patients who tested negative for HepB were given Engerix 40 mcg IM (deltoid) injections at 0, 1, 2, and 6 months. A total of 38 patients with ESRD maintained on APD received vaccinations from 2000-2005 and have hepatitis B surface antibody test results in their medical record. A person with a HepB surface antibody titer less than five was considered as a non-responder.

Overall there were 68.4% male, 57.9% non-black, and 47.4% had diabetes mellitus (DM). Only 28.9% of the patients responded to vaccination.

	Responder	Non-Responder	*P*-value
Age (yrs)	47.8	52.1	0.37
BMI	26	28.7	0.17
Time on dialysis (yr)	2.5	2.3	0.72
Residual Renal Function	0.73	0.6	0.6
Total Kt/V	2.33	2.2	0.12
Serum Albumin (gm/dl)	3.61	3.22	0.06
Serum Ferritin (ngm/ml)	283	298	0.92
Hemoglobin(gm/dl)	11.6	11.3	0.66

Vaccination response rates were high in females (6/12 vs 5/26; p=0.05) and blacks (7/16 vs 4/22; p=0.08). Only 2/18 patients with DM responded compared to 9/19 non-diabetic patients (p= 0.03).

The seroconversion rates for patients with ESRD maintained on APD at our institution was documented to be 28.9%. This result is much lower than the expected published rate of positive conversion of 49% to 72.7%. Male gender, non-blacks, and history of DM are associated with a poor response to hepatitis-B vaccination in this group of patients.

FOCUSED TECHNIQUES CAN IMPACT PERITONITIS RATES: MAKING THE ISPD GOAL ACHIEVABLE

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When ISPD published the peritonitis goal of 1:48 patient months, our average rate was 1:27. In order to reach the new target, we reviewed our procedures; looking for opportunities to improve our peritonitis rate.

Following is a list of the methods or techniques we implemented, with the goal to meet or exceed the ISPD standard. The first change was to develop a consistent connection method for all patients and staff. This was implemented in the fall of 2005 with all new patients. Existing patients were also re-educated on the new technique with return demonstration required. Connection technique was then reviewed with all patients bi-annually during regular clinic visits. Our second intervention was to re-educate patients on peritonitis prevention, through use of our specific hand washing procedure and proper aseptic technique. This was accomplished through demonstration and completion of a written test. Finally, all patients on Automated Peritoneal Dialysis were educated on the use of the Compact Exchange Device to connect their solution bags.

In September of 2005, our cumulative peritonitis rate was 1:27 patient months. Following our focused efforts, our peritonitis rate continually improved, and reached 1:60 patient months in September 2006.

When the ISPD goal for peritonitis was published, we questioned whether the rate was achievable. With review of our practice, we identified three specific interventions which we felt would make a positive impact. These interventions, along with continual reinforcement have proven effective in improving our peritonitis rates, enabling us to exceed the ISPD goal.

EFFICACY OF ICODEXTRIN IN PERITONEAL DIALYSIS PATIENTS: A SYSTEMATIC REVIEW

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Icodextrin is increasingly used in peritoneal dialysis patients during the long dwell to enhance the ultra filtration rates. We aimed to assess the efficacy of Icodextrin in comparison to glucose containing solution in peritoneal dialysis patients.

MEDLINE and CCTR were searched for randomized controlled trials comparing the efficacy of Icodextrin (used in long dwell) with glucose based solution in peritoneal dialysis patients. Two reviewers independently assessed trial quality and extracted data. Results were expressed as weighted mean difference (WMD) for continuous and as relative risk (RR) for dichotomous outcomes with 95% confidence intervals (CI) using a random effects model.

Ten randomized clinical trials were included in this review. Use of Icodextrin in long dwell, in comparison to glucose based solution resulted in higher ultra filtration rates (6 studies, 590 patients, WMD 289.98 ml, 95%CI 59.44 to 519.99), better creatinine clearance rates (3 studies, 306 patients, WMD 0.53 ml/min, 95%CI 0.32 to 0.75), and higher urea clearance rates (3 studies, 306 patients, WMD 0.45, 95%CI 0.24 to 0.66). Mean serum sodium was lower with the use of Icodextrin than glucose based solution (3 studies, 273 patients, WMD -2.00 mmol/l, 95% CI -2.91 to -1.09).

Overall, Icodextrin use resulted in higher ultra filtration rates when used during the long dwell. Separate, long term studies including patients with different peritoneal characteristics (high, high-average, low-average and low transporters) are warranted.

FREQUENCY OF HB TESTING AND ANEMIA DIAGNOSIS IN PATIENTS WITH CHRONIC KIDNEY DISEASE DURING PRE AND POSTDIALYSIS PERIOD

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Objective: This study was conducted to understand the association between timing and frequency of Hb testing, and diagnosis and treatment of anemia in patients with chronic kidney disease (CKD) both prior to and following dialysis initiation. **Methods:** The Medstat Marketscan® claims database (01/00 – 06/05) was queried to identify patients ≥18 years of age with at least one claim for hemodialysis. All patients were required to have at least 24 months of continuous enrollment prior to dialysis and at least one month postdialysis. Hb testing was identified through CPT codes. Anemia was defined by either diagnosis (≥2 claims with ICD-9 diagnosis) or treatment (≥1 claim for erythropoeisis stimulating agent - ESA). Patients were grouped based on timing of anemia identification, either prior to dialysis initiation (Group 1), or after (Group 2). **Results:** Of the 5848 patients with CKD, 51.8% were in Group 1 and 26.5% were in Group 2. A greater proportion of patients in Group 1 had anemia identified by diagnosis than Group 2 (57% vs. 33%). Although both groups were observed prior to dialysis, Group 1 had more frequent Hb testing during that period than Group 2 (mean annual Hb tests: 6.8 ± 8.6 vs 2.4 ± 3.2, respectively). Once anemia was identified, the median time to initiation of ESA treatment was considerably longer for Group 1 than Group 2 (134 vs 53 days). **Conclusions:** These data demonstrate an association between the diagnosis of anemia and the frequency of hemoglobin testing in predialysis patients. Treatment with an ESA did not immediately follow the diagnosis of anemia. Although causality between testing and diagnosis can not be determined, the data suggest that increased attention to obtaining and responding to hemoglobin levels may lead to improved anemia management in this vulnerable population.

FOUR-YEAR FOLLOW-UP OF A COHORT OF PATIENTS WITH ADVANCED CKD MANAGED IN AN ACADEMIC CKD CLINIC: GROUNDS FOR OPTIMISM.

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Individuals with Chronic Kidney Disease (CKD) stages 4 and 5 have a high mortality rate and progress rapidly to renal replacement therapy. We report an extended follow up of a cohort of patients with advanced CKD with the main objective of examining the mortality rate and the proportion of patients in whom the Glomerular Filtration Rate (GFR) can be maintained stable despite advanced CKD.

A total of 102 unselected CKD patients consecutively referred for anemia management were prospectively followed up for four years. 71 subjects (69.6%) were stage 4 and 31 subjects (30.4%) were stage 5 CKD. Time 0 was defined as the time of initiation of erythropoietin therapy. The primary outcomes measured were the initiation of renal replacement therapy (dialysis or transplantation) or death.

At the end of follow up 77 subjects (75.5%) had developed a primary outcome: 61 initiated renal replacement therapy (54 dialysis, 7 transplantation) and 11 died. In the 25 subjects (24.5%) who did not develop a primary outcome the GFR remained stable over the follow up period (23.5$\pm$4.36 at time 0 vs. 21.7$\pm$11.23 ml/min/1.72 m^2 at the end of follow up, p=0.38). There were no differences in the hemoglobin levels and blood pressure levels at the beginning of follow up between groups. The GFR at baseline was associated with adverse outcome (23.5$\pm$4.36 vs. 17.4$\pm$5.24 ml/min/1.72 m^2 in subjects without and with outcomes, respectively, p<0.001). Only 11 subjects died during the follow up period, which represents a standardized mortality rate of 4.59 per 100 person-year. This rate is much lower than previously reported.

We conclude that comprehensive nephrological care in patients with advanced CKD may have a positive impact on mortality rate and delays the initiation of renal replacement therapy. Moreover, in about 25% of patients the GFR remains stable despite advanced CKD.

SAFETY AND TOLERABILITY OF C.E.R.A. (A CONTINUOUS ERYTHROPOIETIN RECEPTOR ACTIVATOR) IN PATIENTS WITH CHRONIC KIDNEY DISEASE: POOLED DATA FROM TEN PHASE II-III TRIALS

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This analysis of 10 phase II-III clinical trials reviews the safety and tolerability of C.E.R.A. for treating anemia of chronic kidney disease. Pooled data from the 4 phase II and 6 phase III trials provided an overall safety population (n=2737) with risk factor profiles (including prevalence of hypertension, diabetes, and congestive heart failure) that were similar to previous studies in this therapeutic area. Patients received C.E.R.A. (n=1789) or a comparator drug (epoetin alfa/beta [EPO] or darbepoetin alfa [DAR]; n=948). In phase III studies, C.E.R.A. was administered IV or SC Q2W for 24 or 28 weeks (Hb correction; range 11-13 g/dL) or Q2W or Q4W for 36 or 52 weeks (Hb maintenance; range 10-13.5 g/dL). Comparator drugs were administered Q1W to TIW (EPO) or Q1W or Q2W (DAR). In phase II studies, C.E.R.A. was administered Q1W, Q2W, Q3W, or Q4W for 12-21 weeks. The phase II safety population had no reference group.

The percentage of patients experiencing ≥1 AE was similar between C.E.R.A. and reference groups (89% vs 91%). The majority of AEs were mild or moderate in intensity, and both groups averaged ~5 AEs per patient. The most frequent (≥10%) AEs, common to both groups, were hypertension, diarrhea, and nasopharyngitis. Rates of serious AEs (37% vs 40%) and AEs leading to withdrawal (3% vs 2%) were similar between C.E.R.A. and comparator groups. The most frequent AEs of special interest were hypertension (13%), vascular access thrombosis (10%), arrhythmia (8%), and congestive heart failure (5%), showing the same incidence between groups. No association was found between AEs and Hb level and rate of rise, except for Hb levels >13 g/dL and vascular access thrombosis in both treatment groups. C.E.R.A. was well tolerated in phase II-III trials, with a safety profile similar to reference drugs.

EFFECT OF PHARMACOLOGICAL SUPPRESSION OF SECONDARY HYPERPARATHYROIDISM ON CARDIOVASCULAR HEMODYNAMICS IN PREDIALYSIS CKD PATIENTS – A PRELIMINARY OBSERVATION

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Cardiovascular events are the principal cause of mortality in CKD patients. Secondary hyperparathyroidism (HPTH), a common complication of CKD contributes to cardiac dysfunction. This study is an attempt to demonstrate the effects of parathyroid suppression with oral calcitriol on cardiovascular hemodynamics.

Twenty adult (>18 years) predialysis CKD patients (stages 3&4) with severe secondary HPTH (iPTH> 180 pg/ml), and creatinine clearance of 15-60 ml/min were given calcitriol (0.5-1μg/d) for 12 weeks (Group1). Ten similar patients received placebo (Group2). Patients on renal replacement therapy, patients with rhythm disturbances, structural heart disease, and acute illness were excluded. CBC, blood urea, serum creatinine, creatinine clearance, calcium, phosphate, alkaline phosphatase, intact PTH levels, and echocardiographic assessment of cardiac function was done at baseline and after 12 weeks of treatment.

Calcitriol effectively suppressed HPTH in treatment group (549.0±378.66 to 341.55±182.48, p=0.001) while no change was seen in placebo group. After 12 weeks, there was no significant change in systolic parameters like LV end-diastolic diameter (Group1- 4.86±0.48 to 4.81±0.52, Group2- 4.78±0.39 to 4.74±0.35), endsystolic diameter (Group1- 2.86±0.33 to 2.78±0.31, Group2- 2.73±0.40 to 2.75±0.40), fractional shortening, septal thickness, systolic volumes, or ejection fraction (Group1- 53.54±3.57 to 53.98±5.29, Group2- 54.32±2.84 to 52.62±3.91) in both groups. However, significant improvement in diastolic parameters namely A velocity (0.696±0.089 to 0.680±0.084, p=0.001) and E/A ratio (1.193±0.210 to 1.238±0.180, p=0.001) was seen in calcitriol group but not in placebo group.

Secondary HPTH is an important factor in pathogenesis of cardiac dysfunction in CKD. There is previous evidence to support that correction of HPTH can improve systolic dysfunction in dialysis dependent patients. This study shows that diastolic dysfunction seen in predialysis CKD patients can also be improved with calcitriol therapy.

NGAL AND EXTRACELLULAR MATRIX PROTEINS IN TGF-BETA INDUCED CHRONIC RENAL FIBROSIS

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Diagnosis and monitoring of chronic renal disease remains based on serum creatinine and albuminuria. Urinary markers for acute kidney injury are being developed but their validity in chronic renal disease is uncertain. Transforming growth factor-beta (TGF-b) is a central mediator of chronic-progressive fibrosis. The Albumin-TGF-b1 transgenic mouse (TG) model is characterized by glomerulosclerosis and tubulo-interstitial fibrosis.

We examined urine of these mice prior to (2 weeks of age) and after (4 weeks of age) the development of fibrotic changes. The results were cross-examined in another model of progressive renal fibrosis, the remnant rat model, 2, 4, and 6 weeks after surgery. Urinary protein was purified using cellulose membrane filters. Proteome composition was determined using 1D PAGE/Western blotting, and 2D gel electrophoresis/Mass spectrometry (MS). To compare urinary excretion with tissue expression, renal mRNA and protein levels of individual gene products were determined.

We found collagen I and VI mRNA and protein expression and urinary excretion strongly increased in TG kidneys compared with WT at 4 weeks of age paralleling the progression of albuminuria. Major Urinary Protein-2 (MUP-2) excretion in the urine strongly decreased in TG mice with disease progression, which was associated with a reduction of production in live and kidney. Urinary Lipocalin-2/NGAL increased as expected, but Lipocalin-2 production also increased dramatically in liver and kidney tissue.

These results indicate that urinary excretion of gene products can be used to monitor intrarenal expression for certain gene products. In addition, increased Lipocalin excretion may be at least partially secondary to increased production in the liver, and examination of the urinary proteome may provide new insights into mechanism and possible markers for progressive renal fibrosis.

CHRONIC KIDNEY DISEASE (CKD) IN PATIENTS WITH NEPHROLITHIASIS: EXPANDED DATA

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The prevalence of CKD in patients presenting with nephrolithiasis is not well documented, and it has been suggested that nephrolithiasis may represent a possible risk factor for CKD.

We reviewed records of 388 adult patients with nephrolithiasis evaluated in the Nephrology Clinic at Cleveland Clinic Florida from Summer/2002 to Summer/2006. 11 patients were excluded from the analysis because of incomplete data. 377 were evaluated for CKD stages I-V according to the National Kidney Foundation (NKF) CKD classification by MDRD glomerular filtration rate (GFR) and presence of kidney damage. 65.3% had some degree of CKD: stage I: 10.9%, stage II: 31%, stage III: 21%, stage IV: 2.1%, stage V: 0.3%.

The prevalence of CKD in our population is significantly higher ($p<0.05$) than the corresponding prevalence in the general population (NHANES 1999-2000).

Only 14.6% of the population had a prior documented history of CKD.

When controlling (by logistic regression analysis) for effects of age, gender, hypertension (HTN), diabetes mellitus, hyperparathyroidism, obstruction and urinary tract infection, the only variables that were significantly correlated with the presence of CKD were age (OR=1.02, P=0.036) and HTN (OR=2.7, P=0.00008). These results support a subset study done previously.

We conclude that: 1) CKD is a common finding in patients presenting for a metabolic evaluation of nephrolithiasis; 2) Most patients with nephrolithiasis found to have CKD had not been previously diagnosed with CKD, despite their referral from another medical provider; 3) The concomitant presence of HTN and nephrolithiasis may be a risk factor for CKD.

Nephrolithiasis and its prevention may play a role in the onset and progression of CKD. Further studies are needed for more conclusive recommendations.

RENAL FAILURE FROM RAAS BLOCKADE IN CKD PATIENTS: A PROSPECTIVE 50-MONTH ANALYSIS - A CALL FOR PRAGMATIC CAUTION TO OPTIMIZE CARDIORENAL PROTECTION WITH RAAS BLOCKADE

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Purpose of study: Despite proven cardiorenal protection from RAAS blockade (AB), the ESRD epidemic with increasing AB use, has raised concerns about iatrogenic ESRD. We hypothesized that iatrogenic ESRD from AB, is unrecognized and poorly understood.

Methods: From 09/2002-02/2005, we prospectively enrolled all CKD patients with increasing serum creatinine (SCr), while on AB. Standard nephrology care was applied. Often, AB was discontinued.

Results: 100 Caucasian patients were enrolled. Late-onset renal failure from AB (LORFFAB), occurred in 5 CKD patients, 1 male, 4 females, mean age 68 years, with normal renal arteries, on stable AB >3 months, without precipitating factors. Duration of stable AB was 34.6 months. Thirty-one months after AB was stopped, SCr fell from 3.4 +/- 1.1 to 2.1 +/- 0.6 mg/dL (p=0.049); one required temporary HD. Twenty-six other patients had RAS (>70%). Precipitating factors occurred in 11, none in 15. Five developed ESRD; 4 died on HD. Of the remaining 21, SCr fell from 2.4 +/- 0.9 to 1.7 +/- 0.6 mg/dL (p=0.006), 25.1 months after AB was stopped. Baseline SCr was significantly higher in the ESRD vs non-ESRD group (2.1 +/- 0.6 vs 1.5 +/- 0.4 mg/dL, p=0.013).

Conclusions: This is the largest prospective analysis of CKD patients with renal failure/ESRD on AB. Renal failure/ESRD from AB remains under-recognized. RAS is a significant risk factor for AB-associated renal failure/ESRD. LORFFAB is a new syndrome, explained by microvacsular RAS, not demonstrable on MRA/angiography. AB-associated renal failure/ESRD, in general, calls for further study. eGFR in CKD patients on AB, must be monitored indefinitely. With accelerated renal failure, with/without RAS, with/without precipitating factors, trial discontinuation of AB is a viable therapeutic option. Such pragmatic application of AB will optimize cardiorenal protection.

RAAS BLOCKADE CAUSING RENAL FAILURE IN CKD PATIENTS WITH RENAL ARTERY STENOSIS: A PROSPECTIVE MAYO HEALTH SYSTEM CLINIC 50-MONTH ANALYSIS

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Introduction: Despite proven cardiorenal protection from RAAS blockade (AB), the ESRD epidemic with increasing AB utilization has raised concerns about iatrogenic ESRD. We hypothesized that renal failure/ESRD from AB in CKD patients with RAS is under-recognized and poorly understood.

Methods: From 09/2002-02/2005, we prospectively enrolled all CKD patients with increasing serum creatinine (SCr), while on AB. Standard nephrology care was applied. Often, AB was discontinued. RAS is defined by >70% narrowing by MRA.

Results: 100 Caucasian patients were enrolled. Twenty-six of them, 9 males, 17 females, mean age 75.3 years, demonstrated RAS – hypertension (13) and DM/hypertension (12). Mean duration of AB was 20.2 months. Lisinopril was prevalent (12/26); mean dose 36 mg/d. Precipitating factors occurred in 11, none in 15. Five developed ESRD; 4 died on HD in one year, one was lost to follow-up. Of the remaining 21, SCr fell from 2.4 +/- 0.9 to 1.7 +/- 0.6 mg/dL (p=0.006), 25.1 months after AB was stopped. 2/21 patients required temporary HD. Renal PTA/stenting (RPTAS) was carried out in 9/21 patients. There was anemia (17/26), hyperparathyroidism (16/26) and hyperkalemia (4/26). Baseline SCr was significantly higher in the ESRD vs non-ESRD groups (2.1 +/- 0.6 vs 1.5 +/- 0.4 mg/dL, p=0.013).

Conclusion: We have reported the largest prospective analysis of renal failure/ESRD in CKD patients with RAS, on AB. This is under-recognized. Precipitating factors are often not present. ESRD can complicate 20% of such events; one-year mortality with ESRD approaches 100%. Discontinuation of AB can lead to significant renal salvage; in selected patients, RPTAS improves renal/other clinical outcomes. Baseline SCr >2.0 mg/dL, imposed higher ESRD risks. In older patients (with RAS), dose maximization of AB, increases the risk of ESRD. We conclude that such pragmatic application of AB, in the older population, will only further optimize cardiorenal protection.

FACTORS INFLUENCING NEPHROLOGY REFERRAL IN MODERATE TO SEVERE CHRONIC KIDNEY DISEASE

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In US adults the prevalence of moderate to severe chronic kidney disease (CKD) i.e. National Kidney Foundation stages 3-5 (estimated glomerular filtration rate- eGFR < 60 ml/min/1.73m²) is 4.7% (8.3 million), while the prevalence of end stage renal disease (ESRD) is only 340,000. It was suggested that timely Nephrology referral may reduce mortality in CKD. We tested for factors affecting referral to Nephrology in a retrospective cohort of 1325 patients (95% male and 5% female) from October 2005 to April 2006, with at least two eGFR values, maximum of < 60 ml/min/1.73m² within a period of 12 months. Patients on dialysis or with a renal transplant were excluded. Primary care provider (PCP) type was 80.7% (1069) MD, 14.9% (198) Physician Assistant (PA) and 4.4% (58) Nurse Practitioner (NP). Compared to patients without renal visits (n=1113) those with renal visits (n=212) were younger (72.6±10.6 vs. 75.8±8.9 years), had lower eGFR (36.7±11.6 vs. 46±9.1 ml/min/1.73m²), higher serum creatinine (2.7±1.4 vs. 1.7±0.6 mg/dL) and higher serum albumin (3.5±1.5 vs. 2.7±2 g/dL) all at p<.001. Renal visits occurred in 15% of MD, 28% of NP and 18% of PA patients (p<.05). On post hoc analysis NP patients had more renal visits than MD patients (p<.05). Patients with renal visits had more advanced CKD stage than those without (74% stage 3, 23% stage 4, 3% stage 5 vs. 94.6% stage 3, 5% stage 4, 0.4% stage 5, p<.001). After correcting for eGFR, patients with ≥1 hospitalizations were 3.6 times more likely to have renal visits than those without hospitalizations (OR 3.6, 95%CI 2.6-5). The farther away patients lived the lower the percentage with renal visits (p<.001, Jonckheere-Terpstra trend test). eGFR decline from the maximum value in the 12 month period prior to the study was similar in patients with and without renal visits (2.6±6.7 vs. 1.7±5.8, p=.07), but increase in serum creatinine was higher in those with renal visits (0.6±0.9 vs. 0.1±0.4 mg/dL, p<.001). In conclusion, age, stage of CKD/ eGFR, serum- creatinine, creatinine increase and albumin, PCP type, prior hospitalization and distance from the renal clinic may influence patient referral to nephrologists.

HIGHER HEMOGLOBIN TARGETS AND KIDNEY DISEASE PROGRESSION: A SYSTEMATIC REVIEW

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Progression of chronic kidney disease (CKD) may be halted by increasing hemoglobin levels through better perfusion of the kidneys. Few observational studies have sustained this hypothesis. We intended to analyze the impact of high hemoglobin targets (>12 g/dl) on the progression of chronic kidney disease.

MEDLINE, EMBASE, and CCTR were searched for randomized controlled trials analyzing the impact of high hemoglobin target on the progression of CKD. Two reviewers independently assessed trial quality and extracted data. Results were expressed as weighted mean difference (WMD) for continuous and as relative risk (RR) for dichotomous outcomes with 95% confidence intervals (CI) using a random effects model.

Seven randomized clinical trials were included in this review. CKD patients maintained with high hemoglobin targets (>12 g/dl) and low hemoglobin targets (<12 g/dl) had similar risk of developing renal replacement therapy (5 trials, 2416 patients, RR 1.02 95%CI 0.77 to 1.35). Similarly patients with both higher and low hemoglobin targets had similar creatinine clearance at the end of the study period (6 studies, 877 patients, WMD -2.33 ml/min, 95% CI -4.89 to 0.23).Doubling of serum creatinine did not differ between the higher and lower hemoglobin group in one study.

Maintenance of higher hemoglobin targets does not prevent the progression of CKD and the need for renal replacement therapy. Thus caution should be exercised in maintaining higher hemoglobin targets.

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IMPACT OF CO-INSURANCE ON OUT-OF-POCKET COST BURDEN FOR PATIENTS WITH CHRONIC KIDNEY DISEASE

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Purpose: Compared out-of-pocket cost (OOP$) burden for CKD patients with versus without co-insurance.

Methods: Data for years 2002 through 2004 were obtained from a managed care database that captures person-specific clinical utilization and expenditures. In each year, these data represent ~ 6 million insured employees and their dependents. Patients who had 2 diagnoses of CKD at least 30 days apart were selected. Comparison groups were patients with diabetes (without CKD) and adult enrollees with an insurance claim. Total annual per-patient OOP$ were calculated as sum of co-payments, coinsurance and deductibles for all claims. OOP$ were compared for patients whose benefit plans required in-network coinsurance with patients whose plans did not require any coinsurance.

Results: The proportion of patients with CKD who made coinsurance payments for their erythropoietic therapy increased from 4% in 2002 to 27% in 2004. OOP payments for patients in co-insurance design plans were nearly twice that of patients not in co-insurance plans (Table 1).

Table 1. Annual Patient OOOP $ by Coinsurance Benefit Design

Patient cohorts	No Coinsurance	Coinsurance (in network)
	Mean (75^{th}, 90^{th})	Mean (75^{th}, 90^{th})
CKD Cohorts		
CKD w/o diabetes	759 (948, 1582)	2022 (2527, 4035)
CKD with diabetes	902 (1218, 1773)	2276 (3082, 4476)
Control Cohorts		
Diabetes (w/o CKD)	532 (693, 1100)	1,384 (1846, 2880)
All Utilizers	243 (303, 569)	749 (1105, 2017)

Conclusions: CKD patients are spending more for healthcare than the average patient and more than patients with diabetes. OOP expenses are significantly higher for patients with insurance plans requiring coinsurance. The trend toward coinsurance requirements may limit the affordability of necessary treatments for patients with CKD.

COMPUTERIZED ANEMIA MANAGEMENT PROGRAM (CAMP©) DOSING OF ONCE MONTHLY DE NOVO DARBEPOETIN ALFAVERSUS BODYWEIGHT-BASED DOSING.

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Monthly (QM) Darbepoetin alfa (DA) has been shown to be effective for the treatment of anemia of CKD. (Ling et al. Clin Nephrol, 2005). Recent studies, however, have shown that normalization of hemoglobin with erythropoietin stimulating agents (ESA) may increase cardiovascular and ESRD risk in CKD (Singh et al. NEJM, 2006 and Drüeke et al, NEJM 2006). This study was to determine the efficacy of QM DA delivered using CAMP©. Also, this study would elucidate whether there were differences between conventional weight-based DA dosing and the CAMP© dosing regimen.

CAMP© was deployed to facilitate treatment of ESA-naïve CKD stage 3–5 patients with i.v. or oral iron and QM DA. Dosing was determined by entry hemoglobin (Hb) rather than bodyweight, according to a computerized algorithm. The therapeutic goal was to maintain Hb in the specified range of 11–13 g/dL. Individual serum iron, transferrin saturation (TSAT), ferritin, Hb and DA dose were obtained QM. Age (y), bodyweight (kg), presence/absence of proteinuria and diabetes were also recorded. Exclusion criteria included receipt of an organ allograft, active immunosuppression and ESRD status. Data were reported as means±SD. Data analysis was by ANOVA and paired 2-tail t-test.

Mean followup of (n=68) patients was 301±74 d and the mean number of DA doses was 9.2±2.6. Hb goal was achieved in 60.3% of patients. Hb>13 g/dL occurred in only 1.5%. The mean initiation doses by bodyweight versus CAMP© were 157.6 mcg and 97.8 mcg, respectively (difference 59.8 mcg $p<.0001$). The mean maintenance dose by CAMP© was 23.7 mcg less than the suggested weight-based dose ($p=.015$). Multivariate analysis showed no interaction between the last maintenance Hb and diabetes, proteinuria, weight, or any combination of the three.

We conclude that CAMP© effectively managed the anemia of CKD in non-ESRD patients with a low probability of overshooting the Hb goal. This approach may abrogate the increased cardiovascular, renal and mortality risks that may be associated with normalization of Hb in CKD. Moreover, the mean Hb-based QM DA algorithmic dose Hb was significantly less than that calculated by weight-based dosing. Presence of diabetes and/or proteinuria and weight had no impact on the last maintenance hemoglobin. The use of weight-based dosing for initiation of DA would likely increase the mean Hb of our trial population, but possibly at the expense of exceeding the target Hb range.

CHRONIC KIDNEY DISEASE PATIENTS AND RENAL TRANSPLANT RECIPIENTS HAVE AN INCREASED INCIDENCE OF MONOCLONAL GAMMOPATHIES.

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The nephrotoxicity of monoclonal free light chains (FLC) is well described. Most commonly they result in tubulointerstitial lesions, but renal amyloidosis and light chain deposition disease are other pathological complications. Less commonly intact immunoglobulins can result in renal injury. Recently a highly sensitive immunoassay (FREELITE™) has become available for quantitatively assessing FLCs in the serum. This assay in combination with protein electrophoresis was used to screen two populations of patients with chronic kidney disease and a population of renal transplant recipients for evidence of monoclonal gammopathies of undetermined significance (MGUS).

The demographics, mean serum creatinine and results from the patients, over 50 years of age, are shown in the Table. The three patient groups had significantly raised incidences of MGUS compared with the published incidence of 3.2 percent in the general population of over 50 years old (Kyle R *et al*, NEJM'06). Both CKD populations had significant proportions of monoclonal FLCs associated with the MGUS, but this was not seen in the transplant patients.

In conclusion, renal transplant recipients and patients with CKD had increased incidence of MGUS. Further work is required to determine whether these monoclonal gammopathies could be involved in the pathology of progressive renal damage in some patients.

	CKD – 1 (n-289)	CKD – 2 (n-306)	Transplants (n-265)
Mean age	60.6	61.4	67
Male %	57	65	61
Mean creatinine umol/L	215	N/A	180
MGUS prevalence	10.4	10.7	10.7
FLC MGUS prevalence	2.8	7	0.8

UNIQUE RECEPTOR INTERACTION PROLONGS THE IN VIVO HALF-LIFE OF CONTINUOUS ERYTHROPOIETIN RECEPTOR ACTIVATOR

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Continuous erythropoietin receptor activator (C.E.R.A.), an innovative agent being developed for treatment of renal anemia, has an in vivo half-life of ~135-138 hours versus ~8 hours for recombinant epoetin. We report here the results of in vitro studies on receptor interaction, stimulation of proliferation, and consumption of C.E.R.A. Binding was assessed by competition of ^{125}I-epoetin (EPO)-β in the UT-7 human myeloid leukemia cell line. Proliferation and differentiation responses to C.E.R.A. and EPO-β were determined in the UT-7 cell line and in purified $CD34^+$ human cord blood and bone marrow cells. Consumption of CERA and EPO-ß was tested in the medium of cultured UT-7 cells. In UT-7 cells competition of radiolabelled EPO-β resulted in IC_{50} values of 200 nM for C.E.R.A. and 1.5 nM for EPO-β. Their in vitro cell stimulating activity is characterized by EC_{50} values of 30-60 pM for EPO-β and 300-500 pM for C.E.R.A. C.E.R.A. similarly had a ~43-fold higher EC_{50} value than EPO-β for expansion of $CD34^+$ erythroid cells (2.81 vs 0.076 nM, respectively). Both agents maximally activated UT-7 cells to the same extent. At concentrations almost maximally stimulating UT-7 cells (100 pM EPO-β or 1000 pM C.E.R.A.), a 120-hr incubation resulted in a 73% to 84% decrease in EPO-ß concentration, whereas the concentration of C.E.R.A. showed no statistically significant decrease. Thus, C.E.R.A. interacts less strongly with cellular EPO receptors than does EPO-β.
As receptor-mediated cellular consumption is a major means of C.E.R.A. or EPO clearance from circulation in vivo, the reduced receptor interaction of C.E.R.A. underlies its long in vivo half-life. C.E.R.A.'s unique receptor interaction sets the stage for increased in vivo activity as seen in Phase II and III studies.

FABRY DISEASE & THE KIDNEY: THE UNIVERSITY OF CONNECTICUT EXPERIENCE

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Purpose: to review CKD in patients with Fabry disease (FD) evaluated at UCONN. We retrospectively reviewed all patients evaluated for FD at UCONN. Many of these patients are included in the Fabry registry.

A total of 41 patients (20 M and 21 F) were evaluated. One patient was found not to have FD. Thirteen (11 F and 2 M) were lost to follow up and had minimal or no data. These young patients (range 4-47 yrs) were referred to UCONN to establish the diagnosis/carrier status of FD. Thus 27 patients (18 M and 9 F) were evaluated.

Nine F were assessed. None had a renal biopsy. All had an estimated GFR (eGFR) of >60ml/min/1.73m^2 [range S creat 0.6-0.8 mg/dl]. Four/9 had symptom onset at a median age of 13 years. The median 24-hr urinary protein excretion was 196 mg [range: 88-1240 mg/d]. Four/9 had hypertension. One patient was treated with an ACE inhibitor (ace-i) while 2 were intolerant of ace-i/ARB. Three patients were on enzyme replacement therapy (ERT). Three with only minor symptoms declined ERT and 2 had no compelling indications.

Eighteen M patients were assessed. All 18 received ERT, some starting ERT in trials prior to FDA approval of agalsidase-beta. One died of a cardiac arrest weeks after ERT onset. Two/18 had no symptoms prior to initiating ERT. The median age of symptom onset was 17.5 years. The median age at presentation was 27.5 years. Seven/18 patients had renal biopsies for proteinuria and CKD. Median 24-hr urinary protein excretion was 770 mg [range: 124-3440 mg/d]. Median eGFR was 61 ml/min/1.73 m^2, range: 14-128, excluding 1 each HD and PD but including 1 renal transplant. One patient progressed to ESRD 25 months after onset ERT, receiving an LRD renal graft. Nine/18 had hypertension at presentation, with 1 developing it over follow-up. Thirteen patients were treated with ace-i/ARBs.

As anticipated, M Fabry patients had more proteinuria and progressive CKD than F carriers. Ace-i/ARBs were used and tolerated in many male patients treated with ERT.

GROUP VERSUS INDIVIDUAL APPOINTMENTS AND THEIR IMPACT ON KIDNEY DISEASE PROGRESSION IN TYPE 2 DIABETES PATIENTS WHO ATTEND THE CLEVELAND CLINIC FLORIDA

Norma Gonzalez, Laura Byham-Gray, Robert Denmark, Michelle Wein, Riva Touger Decker

The purpose of this retrospective chart review was to compare and evaluate the effectiveness of the group sessions and individual appointments for diabetes management of adults ≥18 years with type 2 DM by measuring chronic kidney disease progression, Glomerular Filtration Rate (GFR) and Creatinine (CR). The pilot study was conducted at an ambulatory care facility and was limited to patients that attended either group for at least 3 visits over a period of 6 months from January 2004 to December 2005. A total of 128 charts were reviewed, 65 from the Shared Medical Appointment (SMA) group and 63 from the Individual Appointment (IA) group. The main outcome measures analyzed were CR and GFR. Results were compared using independent t-test, paired t-tests and ANOVA for repeated measures. There were no significant differences in change in CR from baseline to 6 months when compared by groups ($p=0.081$). There were significant differences on GFR between groups at baseline ($p=0.031$), but no significant difference was found between groups from baseline to 6 months ($p=0.104$). This study suggests that group sessions may be as effective as individualized appointments in controlling kidney disease progression in patients with Type 2 DM, but trials with larger samples sizes with a longer duration are warranted.

CLINICAL INERTIA AND CARDIOVASCULAR DISEASE (CVD) RISK FACTOR MODIFICATION IN CHRONIC KIDNEY DISEASE (CKD)

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CKD significantly increases risk from CVD. Data supports a need to intervene in early stages of CKD to prevent and treat CVD. There is little evidence that this is being achieved. Traditional CVD risk factors were analyzed and therapy in 100 CKD Stage 3 patients, cared for at the NMVAHCS, a healthcare system with electronic medical records, control of cost to patients, availability of nephrologists, and where reimbursement from insurance is not a factor. 96% of patients were men, age: 66±9.1, MDRD eGFR: 42.9±8.9 mls/min and BMI: 31± 9.1. 61% had DM (HbA1c: 7.1±1.4%). 49% were diagnosed with CVD. No difference was found when stratifying diagnosis of CVD by diagnosis of DM or age. 51% of diabetics and 46% of non-diabetics had CVD. 85% were receiving ACEI's/ARB·s (no difference when stratified by DM, CVD, BP). 42% were on beta blockers (BB). BB use was higher in patients diagnosed with CVD (55% vs. 30%, p< 0.05). 69% were on diuretics. 70% of patients did not reach goal BP of <130/80. 98 patients were receiving antihypertensives (2.5±1.1 antihypertensives/patient). 30% of prescribed antihypertensives were high dose, 37% medium and 32% low dose. 81% of patients were not at goal LDL cholesterol (CVD-70 mg/dl, no CVD-100mg/dl). Statin therapy was prescribed in 60% of patients but was not associated with achieving LDL goal or CVD diagnosis. 42% of patients received low doses of statins. Anti-platelet therapy was prescribed in 40% of patients (62% with CVD vs. 19% of patients without CVD, p<0 .05). We conclude that the prevalence of CVD is high in CKD Stage 3, even in the absence of DM and management of CVD in CKD remains unsatisfactory, even when the system has readily available clinical data, specialized care, and cost to patient minimized. "Clinical inertia" or lack of initiation and/or insufficiently intensified titration of medical therapy, such as antihypertensive therapy, statins, and anti-platelet medication, may be associated with lack of achieving CVD risk factor reduction in CKD. Nephrologists must take the lead and work with primary care physicians to decrease CVD risk factors in early stages of CKD.

AFRICAN AMERICANS' KNOWLEDGE AND BEHAVIOR REGARDING EARLY DETECTION OF KIDNEY DISEASE

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Kidney disease is an African American public health crisis. The first survey of African Americans about kidney disease was conducted by the National Kidney Disease Education Program (NKDEP), of the National Institutes of Health, to determine this population's knowledge and behaviors related to kidney disease. Using random-digit dialing, 2,039 African Americans were surveyed from seven states (GA, MD, OH, MS, LA, MO, TN). Even though almost half (43.7%) of the African Americans surveyed had a risk factor for kidney disease (including hypertension, diabetes, or a family history of kidney disease), only 2.8% reported that kidney disease was a top health concern for them. Less than half of surveyed respondents knew the correct definition of kidney disease (48.6%), knew a test to diagnose kidney disease (39.5%), and knew that African Americans were at higher risk for kidney disease (18.1%). Few understood the relationship between hypertension, diabetes, and kidney disease; less than 15% mentioned that kidney disease could be a negative consequence of unmanaged diabetes (13.6%), hypertension (12.1%), or a family history of kidney disease (2.4%). African Americans who were objectively at risk for kidney disease did not always perceive themselves to be at higher risk: 75% of African Americans with risk factors for kidney disease did not perceive themselves to be at higher risk. Only 37.4% of African Americans had ever been tested specifically for kidney disease. This study indicates that kidney disease is not currently perceived as an important health problem for African Americans, that they may not understand fundamental information about kidney disease, and that they are not taking action to prevent kidney disease. As the first national study of this topic, the conclusions are important in creating public health interventions to address this urgent problem and can help the nephrology team, including social workers, in targeting programs to most effectively reach this audience.

LONG TERM FOLLOW UP IN FABRY PATIENTS WITH PROTEINURIC KIDNEY DISEASE

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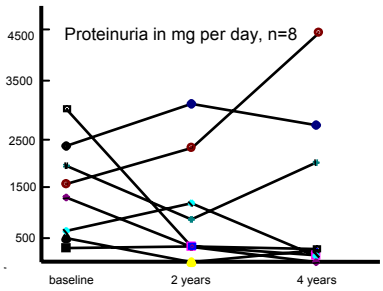
Enzyme replacement therapy (ERT) with recombinant human α- galactosidase A improves clinical symptoms in patients with Fabry disease. We did a long term evaluation of ERT in patients with Fabry disease on chronic kidney disease (CKD) progression.

Single centre, prospective, open label, treatment study (Fabrazyme® 1 mg/kg BW every second week) in 12 patients (2 females) with a mean age of 42 ± 8 years. Only proteinuric patients (>300 mg/day) are reported. Glomerular filtration rate (GFR) was measured using ^{99}Tc-DTPA and proteinuria in 24 hour urine specimen.

During a mean treatment time of 3.8±1.3 years (range 12-60 months) 1 patient died (at 10 month) and 3 patients CKD stages 4 and 5 progressed to ESRD. The remaining 8 patients showed unchanged rates of proteinuria (baseline 1,439±950 mg/d; 2 year 1,056 ± 1.096; final follow-up 1,256±1,647 mg/day, n.s. see figure). GFR was 91 ± 32 at baseline and 82±36 and 79±38 ml/min/1.73m^2 during follow-up (p=0.01). ACE inhibitor or angiotensin receptor blockers therapy was prescribed but patient compliance was suboptimal. Mean sBP was 116±11 and dBP 71±9 mmHg after 3.8 years.



In conlusion ERT alone does not abrogate proteinuria in patients with advanced Fabry disease and further studies are required to demonstrate the effect of intensified adjunctive antiproteinuric therapy.

UNMASKING OF PERIODIC LIMB MOVEMENTS IN SLEEP DURING TREATMENT OF SLEEP APNEA WITH CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) IN THE CHRONIC KIDNEY DISEASE POPULATION

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The chronic kidney disease (CKD) population has a high incidence of sleep disorders, including sleep apnea (SA) and periodic limb movements in sleep (PLMS). Sleep disorders affect the majority of ESRD pts and result in sleep deprivation, negatively affecting immune function and cardiovascular related outcomes. We have previously shown that PLMS strongly predict mortality in the ESRD population. SA and PLMS often occur concurrently. We previously showed that CPAP therapy improves SA in ESRD pts.

In this study, we investigated whether PLMS are masked by SA in the CKD population and if successful tx of SA with CPAP results in increased appearance of PLMS. Of 18 pts studied, 8 (44.4%) had stage III CKD, 2 (11.1%) had stage IV CKD and 8 (44.4%) had stage V CKD on hemodialysis or peritoneal dialysis. Mean age was 68.3±11.2 yrs. Twelve pts (66.7%) were male and 10 (55.6%) were diabetic and 7 (38.9%) were African American. Mean hematocrit was 37.5%±4.1%.

All pts (N=18) had polysomnography (PSG) diagnosed SA. The mean apnea-hypopnea index (AHI) was 53.8±26.6/hr. All pts also had PSG documented successful tx of SA by CPAP. PLMS were tested for in both baseline and CPAP PSGs. Our data showed that with successful tx of SA with CPAP, 10 pts (55.6%) had increased PLMS, 4 (22.2%) remain without PLMS and 4 (22.2%) had mildly decreased PLMS. The highest increase of PLMS index (PLMSI) was 92.4/hr. Overall, PLMSI increased 326% from baseline of 8.0±12.3/hr to 26.1±30.8/hr with CPAP tx (p=0.019). Arousing PLMS index (APLMSI) also increased from baseline of 3.7±7.1/hr to 11.9±15.9/ hr with CPAP tx (p=0.026).

In conclusion, PLMS and SA are common in the CKD population. SA may mask the underlying incidence and severity of PLMS. PLMS tripled during successful treatment of SA. Despite successful treatment of SA with CPAP, sleep deprivation may persist due to unmasking of underlying PLMS.

EFFECT OF SIROLIMUS VERSUS MYCOPHENOLATE MOFETIL ON THE EFFICACY OF DARBEPOETIN ALFA ON ANEMIA IN RENAL TRANSPLANT RECIPIENTS

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Anemia is a well known complication in renal transplant recipients. Although the primary presumption is impaired erythropoiesis, other factors such as immunosuppressive drugs have been suggested to have a negative impact on anemia. We attempt to determine whether there is a difference between sirolimus(SIR) and mycophenolate mofetil (MMF) on the efficacy of darbepoetin alfa(DA) in treating anemia. We examined 78 pts who received DA consistently over a 3 month interval. Of these pts, 24 were excluded based on one of the following: they did not have consistent hemoglobin(Hgb) monitoring, were hospitalized, transfused, or HIV+. The following table demonstrates the characteristics of the pts as well as our findings.

	SIR	MMF	p-value
Age	52.8	55.7	0.503
Gender	17 M, 14 W	14 M, 9 W	0.656
Race	21 AA, 10 W	13 AA, 10 W	0.399
Iron	50	53.5	0.287
TIBC*	225.5	220.5	0.945
Tsat*	0.24	0.29	0.251
Ferritin*	768	574	0.154
CrCl(MDRD)*	30.75	24.99	0.902
Avg DA	119.2	116	0.768
Avg Hgb	10.34	10.84	0.07

Two-sample t-tests as well as Mann-Whitney tests(for non normally distributed data labeled with *) were used to analyze the data. The pts were similar in terms of age, creatinine clearance, and iron studies. The avg DA dose for SIR pts was 119.2+/-40.9 and for MMF pts was 116+/-39.4. The avg Hgb for SIR pts was 10.34+/-1.01 and avg Hgb for MMF pts was 10.84+/-0.949(p-value=0.07). Our study showed that there was no statistically significant difference in average Hgb between the two groups.

POLYOMA VIRUS INFECTION IN 192 KIDNEY TRANSPLANT PATIENTS UTILIZING AN ALEMTUZUMAB INDUCTION-STEROID-FREE PROTOCOL.

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Introduction: Alemtuzumab (Campath 1-H) is a fairly new monoclonal anti-lymphocyte agent that has been successfully used for transplant induction therapy. No study has described the impact of this therapy on polyoma virus infection in a large number of patients. **Methods:** We transplanted 192 adults under this protocol at WHC during 2004-5. Patients received 1-2 doses of alemtuzumab and IV methylprednisolone as induction followed by maintenance immunosuppression (IS) with MMF and tacrolimus. Visualization of decoy cells on urinalysis was used as a screening test for polyoma virus infection. PCR testing for polyoma virus was performed on urine and blood if decoy cells were persistent. A kidney biopsy was performed for a persistent rise in serum creatinine. Patients with polyoma infection were managed by switching MMF to leflunomide and/or reducing IS. Some patients with low levels of viruria were observed, with gradual reduction of IS over time. **Results:** This cohort has been followed a median of 379 days. Viruria developed in 48 patients (25%). Plasma and urine BK-PCR was performed and followed in 38 patients with persistent viruria; in this group, viremia was present in 20 (10%) at any time point. Biopsy-proven Polyoma nephropathy was seen in two patients (1%). Viruria was more likely to occur in males, recipients of deceased donor kidneys and those with greater HLA mismatches ($p < 0.05$ in all). In response to intervention, viruria decreased in 100 %, and viremia cleared in 95%. Viremia persisted in only one patient following a switch from MMF to leflunomide and reduction in IS. **Conclusion:** The incidence of polyoma infection under an alemtuzumab-induction, steroid-free protocol is comparable to that reported with other IS regimens. Both reduction in IS and conversion from MMF to leflunomide were effective in achieving a favorable response.

THYMOGLOBULIN INDUCTION FOR THE DOUBLE AVOIDANCE OF STEROIDS AND CALCINEURIN INHIBITORS IN LIVING-RELATED KIDNEY TRANSPLANTATION

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Introduction: Calcineurin inhibitors (CI) and steroids have been the main stay of immunosuppression in solid organ transplantation. However, they are associated with significant side effects including nephrotoxicity, hypertension and post-transplantation diabetes mellitus. We report our experience with the use of a unique immunosuppressive protocol that utilizes double avoidance of CI and corticosteroids among low immunological risk living donor renal allograft recipients.

Methods: We began using a double avoidance protocol in live kidney transplant recipients in July 2002. From July 2002 through December 2003, we transplanted 17 patients using basiliximab 20 mg on days 0 and 4 for induction. Three doses of methylprednisolone were given, 500 mg on day 0 and day 1, followed by 250 mg on day 2. Patients were given sirolimus for a trough level of 10-15 ng/ml and MMF 1gram BID. No oral steroids were used. Due to high acute rejection (AR) rates, especially in patients receiving a living-unrelated allograft (LURA), the protocol was modified January 2004. Thymoglobulin 1.5mg/kg on days 0, 1 and 3 rather than basiliximab was used for induction, and LURA were excluded. Comparison was made for AR, graft and patient survival, and renal function at one year after transplantation.

Results: The etiology of ESRD was not statistically different between the two groups. 17 patients received Basiliximab and 17 patients received Thymoglobulin for induction. Graft survival was 88 % and 100% respectively with patient survival at 100 % in both groups . The incidence of AR was 41% and 5.9% in the Basiliximab and Thymoglobulin groups respectively(P value < 0.05)

Conclusion: We have shown that the double avoidance of steroids and CI can be achieved in patients receiving live renal allografts with excellent graft function and survival at one year. The exclusion of LURA along with the use of induction with Thymoglobulin vs. basiliximab resulted in improved AR rates.

ANCA POSITIVE RECURRENT IgA NEPHROPATHY POST TRANSPLANTATION

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The risk of Recurrence of IgA Nephropathy (IgAN) is variable after transplantation, and the only predictor of recurrence was a longer period of time after transplantation. ANCA is an antibody associated with pauciimmune necrotizing and Crescentic GN. Furthermore, a clinical entity of IgA Nephropathy that is manifested as Crescentic GN is rarely associated with ANCA. Case: A 31 yr old lady, recipient of a living related kidney transplant for ESRD from biopsy-proven IgAN, presented 5 years post-transplant with a purpuric rash on her legs; biopsy revealed leukocytoclastic vasculitis, responding to high dose steroids. A year later, patient developed increasing proteinuria and a rising creatinine, with histologic changes consistent with recurrent IgAN with diffuse mesangial proliferative glomerulonephritis, focal segmental endocapillary proliferation and cellular and fibrocellular crescent formation. Her serology was positive for pr3-ANCA, but negative for lupus. She was restarted on steroid therapy. Her renal function remained stable. To assess response, a repeat biopsy done 6 weeks later showed decrease in active glomerular lesions, with increase in glomerular sclerosis, and presence of fibrous crescents. She was then started on Cyclophosphamide IV therapy monthly, which was tolerated poorly. She was re-biopsied, and showed improvement of mesangial proliferative changes, no evidence of necrotizing lesions, and increase in glomerular sclerosis. Her most recent S Cr was 1.4 mg/dL, and a/c ratio corresponded to 0.5 gm /24 proteinuria.

A literature review showed an incidence of recurrent IgAN at 21-58%. Another study showed estimated 10-year graft loss due to IgAN recurrence at 9.7%. There is scarce data on ANCA associated crescentic GN and recurrent IgAN in post transplant patients. In the non-transplant literature, there is an overlap syndrome of ANCA associated Crescentic GN and IgAN that resembles ANCA associated Crescentic GN histologically and its response of treatment with cyclophosphamide and corticosteroids.

HYPOMAGNESEMIA LEADING TO BLINDNESS IN A RENAL TRANSPLANT PATIENT**,** Syed Saghir, Farhan Arif, Michael Cardi, The Christ Hospital, Cincinnati, OH

Posterior Reversible Encephalopathy Syndrome (PRES) is an acute encephalopathy associated with calcineurin inhibitors (CNI) and hypertension. Hypomagnesemia, a common side effect of CNI due to decreased renal tubular re-absorption, has been associated with PRES.

A 49 year old black female, status post renal transplant from a living donor 4 years ago for membranous glomerulonephritis, previously on cyclosporine but switched to tacrolimus 1 month ago, presented with acute onset of confusion, one episode of generalized tonic-clonic seizure and visual disturbance for ten hours. In Emergency Department, the patient was agitated, with a temperature 98.2 ° F and BP of 186/92 mmHg. Pupils were round and reactive to light, but patient was completely blind. The rest of physical examination including neurological examination was normal. A stat head CT was normal. Laboratory data revealed a magnesium level of 1.2 mg/dl, and a normal CBC, Na, K, glucose, BUN, creatinine, phosphorus, Ca, cholesterol and tacrolimus levels. Lumbar puncture was unremarkable. MRI of the brain done immediately, revealed hyper-intense T2 signal compatible with vasogenic edema involving the sub-cortical white matter, and bilateral occipital lobes, suggesting PRES. The patient's BP was controlled, tacrolimus was discontinued and replaced with sirolimus, and IV magnesium given. Vision was restored within 12 hours. A brain MRI done fifteen days later, showed complete resolution of changes.

PRES is a significant complication of immunosuppressive therapy. Typical symptoms include headache, altered mental function, seizures and cortical blindness. MRI reveals edema in the brain, predominantly in the posterior portions of the cerebral white matter, due to hypertensive and/or toxic damage to the wall of blood vessels, and breakdown of the blood-brain barrier. Thompson et al (Lancet 1984) reported hypomagnesemia as a precipitating factor for PRES in patients receiving cyclosporine. Our patient represents an unusual case associated with hypomagnesemia and tacrolimus, not reported previously, and illustrates a serious complication of tacrolimus-associated renal magnesium wasting. The syndrome should be promptly recognized, since it is reversible and readily treated.

MANAGEMENT OF ANEMIA IN POST-TRANSPLANT PATIENTS WITH DARBEPOETIN ALFA

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The prevalence of, and risks for, post-transplant anemia have been described. However, specific details about treatment with darbepoetin (D), including its safety and efficacy, have not been reported. We have previously reported our experience with a nurse-driven protocol to manage our chronic kidney disease patients. Herein we report on a cohort of patients (n=30) with post-transplant anemia, for whom data were collected prospectively and arbitrarily censored at 6 months. Patients referred back to our practice for long-term management after kidney transplantation were enrolled in our nurse-driven anemia management pathway if Hgb $\leq$ 10.5 gm/dl. They were treated with D (25 mcg) every other week, with dose escalations as necessary to achieve target Hgb value of 11-12 gm/dl. The patients' average age was 50$\pm$15 (m$\pm$ SD) years; they averaged 65 months (2-192) after transplant. The cohort included 60% AA and 27% Caucasian. Their baseline creatinine was 2.7mg/dl (1.1-4.7). By CKD stage, 37 % were stage 3, 53 % stage 4, and 10 % stage 5. Sixty % (18/30) were on ACEi and /or ARBs. Responders (20/30, or 66 %) were defined as those who reached target hgb (11-12 gm/dl) within six months. Non-responders (10/30, or 33 %) did not reach target within the time period. The target Hgb was reached in an average of 9 weeks. Once at target Hgb, the average dose of D was 56 $\pm$ 41 mcg every other week. In the responders, the average blood pressure pre-treatment was 132/75mm Hg and by 24 weeks was 127/75 mm Hg (NS). Likewise, serum creatinine remained stable over the specified time period: pretreatment 2.7 $\pm$1.1 mg/dl vs. 24 weeks 2.5 $\pm$1.7 mg/dl (n= 20, p= NS). Adverse events were infrequent, including one episode of relative hypotension and one CVA. Of the ten non-responders, 3 required HD, all of whom had a baseline Scr $\geq$ 3.5 mg/dl. We conclude that the use of a darbepoetin-based anemia management pathway is safe and effective in the treatment of anemia following renal transplantation.

QUALITY OF LIFE RESPONSES FROM LIVING RELATED, EMOTIONALLY RELATED AND PUBLICLY SOLICITED LIVE KIDNEY DONORS OF DIVERSE ETHNICITIES.

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Purpose: Published transplant quality of life literature generally concentrates on white traditional donors. This study evaluated the satisfaction of minority and publicly solicited living kidney donors.

Method: A questionnaire in English and Spanish was sent to 268 traditional live donors (TLD) who donated between January 1, 1999 and December 31, 2003. It was sent separately to 26 live donors who volunteered because of public solicitation (PSD) from 2001 to 2006. Sample questions: “During your evaluation, did you receive adequate information?” “How did your family members react to your donation?”

Results: 75/ 268 (28%) TLD questionnaires were returned. Responses from Hispanics(H) 39%, African Americans (AA)17%. 23/ 26 (88%)questionnaires sent to PSD were returned. Responders and non-responders had similar demographics. Responders: **H**: 48% male, age 19-65years. **AA:** 50% male, age18-59 years. **PSD**: 65% male, age 23-59 years. Education: primary school through college (higher college education in PSD group). Responses were positive; suggestions for improvement included more follow-up after donation, more information on long-term effects of donation and more education in minority communities regarding donation.

Conclusions: Minority and solicited live kidney donors are informed and feel positive about donations.

SINGLE CENTER EXPERIENCE WITH LOW-DOSE THYMOGLOBULIN IN KIDNEY TRANSPLANT PATIENTS

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Thymoglobulin is a polyclonal antibody that has been used as an induction agent in kidney transplantation. The ideal dose for Thymoglobulin is not clear but most centers use 1.5mg/kg/dose for total of 4-10 doses (Total dose: 6- 15mg/kg). We report our single center experience in kidney transplant patients with low-dose Thymoglobulin of 1mg/kg/dose for a total of 3-5 doses (Total dose: 3-5mg/kg).

The study was designed as a retrospective, non-randomized and unblinded evaluation of adult renal transplant recipients at our center. Patients were induced with Thymoglobulin (1mg/kg intravenously) on days 0, 1 and 2. Some patients received more doses depending on the discretion of the physicians. The primary end point of the study was acute rejection rate 12 months post transplant. Also studied were the patient and graft survival, serum creatinine levels, glomerular function rate calculated by the Modification of Diet in Renal Disease (MDRD) formula, polyoma virus nephropathy and malignancies. The dose of Thymoglobulin used was 1.08±0.2 mg/kg/dose. The total number of doses used were 2.88±0.94. The total dose used was 3.02±1.11 mg/kg.

The one year serum creatinine was 1.40±0.45 mg/dL with the MDRD GFR of 56.5±18.11 ml/min. The one year patient survival was 92.1 % and one year death censored graft survival was 96.8 %. The one year acute rejection rate was 6.86 % (n = 7). The other complications included post transplant lymphoproliferative disorder 0.98 % (n =1), Polyoma virus associated nephropathy 0.98 % (n =1), West Nile 0.98 % (n = 1), Cytomegalovirus infection 2.94 % (n =3) and Histoplasmosis 0.98 % (n = 1).

We conclude that low dose Thymoglobulin in kidney transplant patients is safe, cost effective treatment and is associated with a low incidence of acute rejection and very good graft survival rates. Additionally, low incidences of polyomavirus associated nephropathy, lymphomas and opportunistic infections were seen.

LEUKOPENIA IN RENAL TRANSPLANT RECIPIENTS, RISK FACTORS AND COMPLICATIONS

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Purpose: Leukopenia and neutropenia in solid organ transplant recipients has not been well reported. The effect of these conditions on patient and allograft outcomes is also unclear. This study was designed to identify risk factors for leukopenia and to define complications and patient outcomes. ***Methods:*** Retrospective chart analysis was done of 864 patients who received a renal transplant from January 1996 to April 2006 and were followed at our institution. Patients who developed leukopenia (L) (WBC count < 3500/mm^3) were selected and further classified as having mild leukopenia (ML WBC- 3.5-2 K/ mm^3)and severe leukopenia (SL WBC 2 K/ mm^3). Logistic regression analysis was performed to define associations between leukopenia and several transplant factors. ***Results:*** 144 (17%) of the patients had leukopenia of whom 15.3% had neutropenia. 31% of patients developed infections, of these 55% were CMV infections. 16 developed bacterial infections. 6.9% of patients died of sepsis. In a univariate logistic regression model, factors associated with risk of SL were CMV infection, EBVpositive serology and acute rejection episodes. Immunosuppression (IS) regimens in various combinations, bactrim, valgancyclovir, gancyclovir,donor/recipient CMV IgG status and age were not associated with SL. In a multivariate model acute rejection (Odds Ratio 10.07, P<0.001) and neupogen use were the most significant associations with S (Odds Ratio 4.47, P<0.005). ***Conclusions:*** Leukopenia is a significant disorder affecting the management of solid organ transplant recipients. Our study reveals a significant causal relationship between SL, and acute rejection. Surprisingly, IS medications were not associated with leukopenia regardless of dosage. this study highlights the need for closer monitoring in this subset of patients to reduce morbidity and mortality associated with leukopenia.

RHABDOMYOLYSIS AS COMPLICATION OF EHRLICHIOSIS IN A RENAL TRANSPLANT RECIPIENT

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Human ehrlichiosis is an emerging pathogen in immunocompromised patients, potentially leading to increased morbidity compared to immunocompetent recipients . We report the case of a renal transplant recipient with human granulocytic ehrlichiosis (HGE) complicated by rhabdomyolysis. Case: 33 year old renal transplant recipient from 4 months earlier, on triple immunosuppression with Tacrolimus, MMF and steroids (no HMGCoA reductase inhibitors), presented with fever, headache and severe myalgia for 1-2 weeks. Patient stated that he was home most of the time, and recalled no tick bite but his house was surrounded by woods, and that he had an indoor cat with no ticks. Examination revealed a febrile male with chills, dry skin and mucus membranes, clear chest, normal heart sounds, abdomen soft, non-tender, with no organomegaly, and no edema or rash. Admission labs revealed neutropenia (ANC 400), S Cr 3.0 mg/dL, elevated hepatic enzymes (AST 1178/ALT 239/LDH 1237) elevated CK at 96,266 IU/L, and myoglobinuria 20424 µg/L. Blood cultures and CMV Pcr were negative, and chest X ray normal. Broad spectrum antibiotics and aggressively hydration was started, Tacrolimus and MMF stopped, and GCSF given with good response. The patient continued to spike fevers, and peripheral smear showed Ehrlichia morulae in the granulocytes. The patient was switched to IV doxycycline, and started to defervesce. Rhabdomyolysis resolved with hydration, and non-dialytic support, and he was discharged on oral doxycycline. Immunosuppression was slowly increased at subsequent clinic visits. The patient has made a full recovery, with no limitations in his quality of life. We describe, to our knowledge, the first case of HGE in a renal transplant recipient complicated by rhabdomyolysis. Ehrlichiosis can cause significant morbidity in immunocompromised patients and high degree of suspicion for the disease is warranted in such patients for earlier diagnosis.

DEPRESSION, SOCIAL SUPPORT AND MEDICATION SELF-EFFICACY IN OLDER RENAL TRANSPLANT RECIPIENTS

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As chronic renal disease increases in those aged 55 and over, renal transplantation also increases as a life-saving therapy that enhances quality of life, prolongs the lifespan, and reduces care costs. Depression, social support and medication self-efficacy can impact the outcomes of renal transplantation. Older renal transplant recipients are at risk for poor outcomes due to cognitive and physical changes associated with aging. This is the first study to describe the correlation between age and depression, social support and medication self-efficacy in the range of older renal transplant recipients.

The study sample consisted of 50 renal transplant recipients aged 55 years or older in a mid-southern transplant center. Depression was measured with the Beck Depression Inventory. Social support was measured with the Social Support Appraisals Inventory. Self-Efficacy was measured with the Long-Term Medication Self-Efficacy Scale. Mean age was 60.5 years, 62% were females, 50% Caucasian, 30% with high school education, 56% disabled, and 83% received deceased donor kidneys. Six percent were prescribed CyA, 12% FK, 62% MMF/FK, 6% MMF, 6% MMF/CyA, 4% FK/AZA, and 4% MMF/sirolimus. Mean depression score was 2.2 (SD =2.3; range 0-9). Mean social support score was 34.49 (SD =11.14; range 23-78). Mean medication self-efficacy score was 103.58 (SD =10.18; range 100-135).

Age was not correlated with depression (r =.187, p =.198) or social support (r =-.093, p =.527). Age was correlated with medication self-efficacy (r =-.442, p =.001). These findings indicate that older renal transplant recipients are not more depressed and they do not appear to have changes in social support. However, as renal transplant recipients get older, their self-efficacy in taking long-term medications is decreased.

SINGLE CENTER EXPERIENCE WITH LOW-DOSE THYMOGLOBULIN AND STEROID FREE INDUCTION IMMUNOSUPPRESSION IN KIDNEY TRANSPLANT PATIENTS

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Thymoglobulin is a polyclonal antibody that has been used as an induction agent in kidney transplantation. We report our single center experience in kidney transplant patients induced steroid free with low dose Thymoglobulin of 1mg/kg/dose for a total of 3-5 doses (Total dose: 3-5mg/kg).

The study was designed as a retrospective, non-randomized and unblinded evaluation of 46 adult renal transplant recipients at our center. Patients were induced with Thymoglobulin (1mg/kg intravenously) on days 0, 1 and 2. Some patients received more doses depending on the discretion of the physicians. Patients received IV Methylprednisolone 250mg on the day of the surgery. This was rapidly tapered and stopped over the next 6 days. The maintenance immunosuppression included combinations of Tacrolimus, Mycophenolate mofetil, Sirolimus, and Cyclosporine. The primary end point of the study was acute rejection rate 12 months post transplant. Also studied were the patient and graft survival, serum creatinine levels, glomerular filtration rate calculated by the Modification of Diet in Renal Disease (MDRD) formula, polyoma virus nephropathy, opportunistic infections and malignancies. The dose of Thymoglobulin used was 1.03±0.17 mg/kg/dose, the total number of doses used were 3.41±0.54. The total dose used was 3.51±0.84 mg/kg.

Mean serum creatinine at the end of 12 months was 1.27±0.29 mg/dL. Mean MDRD-GFR at the end of 12 months was 59.1±12.5 ml/min. Patient survival was 95.65%. Death censored graft survival was 100 %. Complications included an acute rejection rate of 4 out of 46 (8.69%), Cytomegalovirus infection 2.2 % (n =1), Diabetes mellitus 6.5% (n=3), and Histoplasmosis 2.2 % (n = 1).

We conclude that low dose Thymoglobulin in kidney transplant patients is safe, cost effective treatment and is associated with a low incidence of acute rejection and very good graft survival rates in patients on steroid free protocols.

METABOLIC SYNDROME IN AN OUTPATIENT TRANSPLANT CLINIC POPULATION

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Kidney transplantation is associated with the development of glucose intolerance, dyslipidemia, abdominal obesity, and hypertension, all of which are components of the metabolic syndrome (MS). There is limited information about the prevalence and significance of the development of MS in kidney transplant patients. We conducted a retrospective study among patients attending the Transplant Clinic at Tufts-New England Medical Center who had undergone a kidney transplant between 2000 and 2005, with at least 6 months post-transplant followup. Patient data was collected at 6 months, one and two years post-transplant. Exclusion criteria were type 1 diabetes, severe systemic illness, and dual organ transplant. The mean age of the 161 patients was 50 $\pm$ 13.2 years; 45% of patients were female; 75% were Caucasian; 42% received a deceased donor transplant. Immunosuppression consisted of prednisone, FK-506, and mycophenolate mofetil in 89% of patients. Median time after transplant was 44 months [range 11-82 months]. The prevalence of MS defined by the ATP III criteria was 52%. Diabetes was present in 28.6%; roughly half of them had pre-existing diabetes. The remainder developed it de novo post-transplant. The median time to developing post-transplant diabetes was 6 months [95% CI = 4.40-7.60]. The prevalence of each of the following traits - body mass index (BMI) > 25, hypertension, and hypertriglyceridemia - was each 72%. Pre-transplant risk factors for development of MS included older age [p=0.01], higher BMI [p<0.01], male gender [p=0.03], family history of diabetes [p<0.01], deceased donor source [p=0.02], and primary rather than repeat transplant [p=0.03]. During 24 months of followup, presence of MS was associated with prevalent cardiovascular disease [OR=2.2; 95% CI = 1.01-4.81; p=0.05], but not poorer graft function.

In summary, there is a higher prevalence of metabolic syndrome and its components after kidney transplantation. Prospective studies are required to define its prognostic significance with regard to patient and graft outcomes.

IMPACT OF ANEMIA PRE AND POST-TRANSPLANT ON PATIENT SURVIVAL

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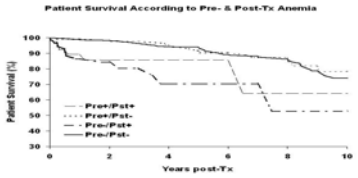
The effect pre and post-transplant (tx) on patient survival has not been fully investigated. We conducted a single center retrospective study of 1051 patients who underwent renal transplantation between 1992 and 2003. We defined anemia as hemoglobin (Hgb) < 10 mg/dl. We evaluated the impact of anemia both pre and post-transplant on overall patient survival. Patients were categorized into 4 groups: 1) Anemic: Pre-Tx Hgb <10 and Mean Post-Tx Hgb <10 (Pre+/Pst+); 2) Anemic pre-tx only: Pre-Tx Hgb <10 and Mean Post-Tx Hgb ≥10 (Pre+/Pst-); 3) Anemic post-tx only: Pre-Tx Hgb ≥10 and Mean Post-Tx Hgb <10 (Pre-/Pst+); and 4) Non anemic: Pre-Tx Hgb ≥10 and Mean Post-Tx Hgb ≥10 (Pre-/Pst-). Multiple, pairwise comparisons between groups were made using the Bonferroni method. Cox regression models were used to assess the effects of pre and post transplant anemia on patient survival. Of the 1051 patients included in our analysis, 23% were anemic pre or post-tx or both. There was no difference in the anemic and non-anemic groups pre and post-tx in regards to race, dialysis pre-tx, donor type and degree of HLA mismatch. Factors like recipient age, gender, post-tx GFR and number of years of pre-tx dialysis that were significantly different between the groups were adjusted for in the multivariate model. Pre-tx anemia did not affect overall patient survival post-tx. However, post-tx anemia was associated with poorer patient survival (Hazard Ratio=2.1, 95 % CI=1 to 4.3, p= 0.02) (Fig. 1).



IMPACT OF ANEMIA PRE AND POST-TRANSPLANT ON RENAL ALLOGRAFT SURVIVAL AND ACUTE REJECTION RATES

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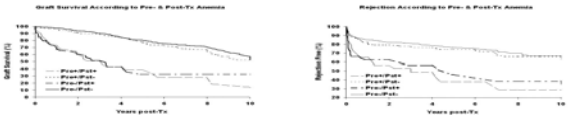
The effect pre and post-transplant (tx) on graft survival and acute rejection is not known. We conducted a single center retrospective study of 1051 patients (Pts) who underwent renal transplantation between 1992 and 2003. We defined anemia as hemoglobin (Hgb) <10mg/dl. We studied the impact of anemia both pre and post-transplant on graft survival and acute rejection rates. Pts were categorized into 4 groups: 1) Pre and post-Tx Hgb <10(Pre+/Pst+); 2) Pre-Tx Hgb <10 and Post-Tx Hgb≥10 (Pre+/Pst-); 3) Pre-Tx Hgb ≥10 and Post-Tx Hgb <10 (Pre-/Pst+); and 4) Pre and post-tx Hgb ≥10(Pre-/Pst-). Multiple, pairwise comparisons between groups were made using the Bonferroni method. Factors likely to affect outcome and which seemed different between groups were adjusted for in Cox regression models. Of the 1051 pts, 23% were anemic pre or post-tx or both. There was no difference in the anemic and non-anemic groups pre and post-tx in regards to race, dialysis pre-tx, donor type and HLA mismatch. Pre-tx anemia did not affect graft survival or acute rejection rates post-tx. However, post-tx anemia was associated with poor transplantation outcomes and retained statistical significance even after adjustment for potential confounders like recipient age, gender, donor age, type of renal allograft, degree of HLA mismatch, post-tx GFR and delayed graft function. Post-tx anemia was associated with poorer graft survival (HR=2.9, 95%CI=2 to 4.1, p<0.0001) and higher rejection (HR=1.4, 95%CI=1 to 2, p=0.03). (Figs 1 and 2) Our study suggests that pts with post-tx anemia are more likely to have acute rejection episodes and have poorer graft survival.



NON-SEROGROUP O1 *VIBRIO CHOLERAE* IN A RENAL TRANSPLANT PATIENT

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Kidney transplant patients are susceptible to a host of life-threatening infections due to induction chemotherapy, maintenance immunosuppression, and anti-rejection treatments. Bacterial organisms comprise the majority of infections in long term transplant patients. Cellulitis, which is usually caused by beta-hemolytic streptococci or staphylococci can cause serious infection in the transplant patient and are usually cleared rapidly with antibiotic therapy targeted to gram positive organisms. Rarely, cellulitis may not respond to conventional antimicrobial therapy. In these situations, unusual pathogens should be suspected.

We report a case of a 29-year-old male who presented with a painful left leg, fever, and rigors for 2-days. He had a history of two deceased donor transplants, the first in 1999 which failed due to noncompliance, and the second in 2004 with delayed graft function. One day prior to symptoms, the patient had gone fishing in the Mazon river near Joliet, Illinois. He had to hike through thick brush to get to the river wearing only sandals and shorts. There was unknown exposure to trauma but the patient had noticed excoriations on his legs after the hike. Blood cultures eventually grew *Vibrio cholerae* which was confirmed by a reference laboratory. The Illinois Department of Public Health confirmed that the *V. cholerae* was in fact a non-serogroup O1 isolate.

The non-O1 *V. cholerae* are distinct non-toxigenic strains that do not agglutinate in type-O1 or O139 antisera. These strains typically do not cause epidemic diarrhea as seen in southeast Asia but usually extra-intestinal infections such as cellulitis, meningitis, urinary tract and pulmonary infection. Many documented cases of these non-O1 strains have environmental exposure to estuarine or coastal topography. Other cases of cellulitis caused by the same organism in Colorado and again in Illinois suggest that the non-O1 *V. cholerae* may be more indigenous to certain inland bodies of water than was previously appreciated. This is the first reported case of *V. cholerae* cellulitis and bacteremia in a renal transplant recipient.

SOCIAL NETWORKS AND AFRICAN AMERICAN PATHWAYS TO KIDNEY TRANSPLANTATION

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The purpose of this study is to determine the relationship between African American dialysis patients' social network composition and their knowledge of kidney transplants. The hypothesis is that getting a kidney transplant is influenced by race and socioeconomic status through social network structure, which influences knowledge and attitudes about kidney transplant and leads to the behavior of getting a transplant workup. In preparation for this study, de-identified information about the race and insurance status of patients in each dialysis unit in the country was acquired from the U.S. Renal Data System 2004 Annual Data Report. Using this data, Chicago area hemodialysis units were selected with the highest case mix of race and income and several dialysis units were identified that have a majority of African American patients with income variation for the study. To confirm that there would be adequate variation in income, interest in kidney transplant, and status in the transplant pathway among African American Chicago-area hemodialysis patients, a pilot study with 32 patients was conducted in May 2006. The pilot study indicated that patients had varied incomes, and interest in kidney transplantation. The pilot study also suggested that African American dialysis patients in the Chicago area are still getting “stuck” on the pathway to kidney transplantation, and corroborates previous research. Almost half (48%) of the patients interested in a transplant never have been seen at a transplant center, and little more than half (55%) of the patients who have actually been seen at a transplant are still not on a kidney transplant list. Out all of the patients in the pilot survey who stated that they are interested in getting a kidney transplant, only 19% of them reported to be active on a kidney transplant list. This study will provide the first information available about African American ESRD patient social networks. This knowledge can be used to better understand racial disparity in kidney transplantation and provide insight that could be used for future social work research on this problem that may be able to decrease the rates of such disparity.

ECONOMIC IMPACT OF GASTROINTESTINAL MEDICATION REDUCTION AFTER CONVERSION FROM MYCOPHENOLATE MOFETIL (MMF) TO ENTERIC-COATED MYCOPHENOLATE SODIUM (EC-MPS).

Paul Bolin, Karen Parker, and Susan Gerkin

Gastrointestinal (GI) medications are commonly used in renal transplant patients due to GI complications associated with immunosuppressive regimens. Previous studies have demonstrated improvement in GI tolerability after conversion from MMF to EC-MPS. The aim of this study was to determine the patient's cost savings from GI medication reduction after conversion to EC-MPS and its impact on quality of life (QOL) as evidenced by Patient-Reported Outcomes (PRO).

Sixty-one renal transplant patients with GI side effects were successfully converted to EC-MPS. All patients were on a GI medication. Forty-one percent were on a PPI and 59% were on a H-2 Blocker. Patients were placed on a protocol to discontinue or reduce their GI medication. Patients were assessed at baseline, 30, and 90 days for GI symptoms and completed three self-administered questionnaires: Gastrointestinal Symptom Rating Scale (GSRS), Gastrointestinal Quality of Life Index (GIQLI) and the Psychological General Well-Being Index (PGWBI). Cost savings due to GI medication reduction were calculated using published average wholesale prices.

Our results show that 87% successfully reduced or discontinued their GI medication without worsening of symptom burden or impacting QOL. A balanced reduction in both PPIs and H-2 blockers was observed. Estimated cost savings per patient for H-2 blockers are $925-$1850 and PPIs are $1861-$3722 annually.

This study suggests that after conversion to EC-MPS, renal transplant patients can successfully reduce GI medication while maintaining their health-related QOL and overall well-being. Considering graft survival rates of 72% at 5 years, this could translate into significant savings for renal transplant patients.

RENAL INFARCTION DUE TO PARADOXICAL THROMBOEMBOLISM: AN UNUSUAL CAUSE OF ACUTE KIDNEY INJURY

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We report an unusual case of acute renal insufficiency due to bilateral kidney infarction caused by paradoxical thromboembolism.

A 38-year-old Caucasian man presented to a local emergency room with sudden onset of right sided flank pain. Initial lab studies were remarkable for elevated lactate dehydrogenase (LDH) 1964 units/L and serum creatinine (Cr) 1.6 mg/dl (baseline Cr = 1 mg/dl). Abdominal CT scan with contrast revealed absence of excretory phase of the contrast from the right kidney. With renal infarction as the probable diagnosis, he was started on heparin drip and transferred to our facility for further management.

He arrived at our hospital about 36 hours after the onset of symptoms. A radioactive hippuran scan showed absence of uptake in the right kidney and a wedge defect in the upper pole of the left kidney. An arteriogram demonstrated filling defects in the distal right renal artery as well as branches of the left renal artery, confirming the mechanism of renal injury as arterial obstruction. There was no evidence of atherosclerotic disease in the aorta but Doppler ultrasound revealed a large thrombus in the right superficial femoral vein. A subsequent transesophageal echocardiogram with bubble study demonstrated a patent foramen ovale (PFO). Thus, the final diagnosis was determined to be renal infarction secondary to paradoxical embolism from the right lower extremity deep venous thrombosis in the setting of an intracardiac shunt. Due to delay in diagnosis past the window of opportunity, therapy directed at renal revascularization was unwarranted. Initial management was supportive and the patient was started on long term anticoagulation.

Renal infarction is an uncommon cause of acute kidney injury and that caused by paradoxical embolism is exceedingly rare. The paucity of reported cases in this regard reflect the under diagnosis of renal infarction largely due to a non-specific clinical presentation and low index of suspicion. The case serves as a useful remainder of the importance of a thorough clinical evaluation and judicious use of laboratory and imaging tests to arrive at the diagnosis expeditiously.

PRIMARY AMYLOIDOSIS IN A RENAL TRANSPLANT RECIPIENT: A CASE REPORT

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Primary amyloidosis is a rare form of plasma cell dyscrasia characterized by tissue deposition of monoclonal immunoglobulin light chains. We describe a patient with primary amyloidosis diagnosed eight years after renal transplantation, raising the possibility that it may be a consequence of immunosuppression.

A 74-year-old Caucasian man presented with painless jaundice and loose, non-bloody stools for two months. He underwent deceased-donor renal transplantation eight years ago for diabetic nephropathy and his immunosuppression regimen included cyclosporine and prednisone. Initial laboratory exam revealed elevated liver function tests (LFTs); AST 147 U/liter, ALT 48 U/liter, total bilirubin 6.2 mg/dl and alkaline phosphatase 1941 IU/liter. He had mild proteinuria (urine protein 819 mg/24 hours); serum creatinine was stable at a baseline of 1 mg/dl.

Review of prior records revealed isolated elevation in alkaline phosphatase to 400 IU/liter with otherwise normal LFTs a year ago. Abdominal CAT scan at that time as well as during this admission revealed diffusely enlarged but otherwise unremarkable liver and normal pancreatico-biliary system. Enteroscopic retrograde cholangio-pancreatiography (ERCP) did not show any evidence of pancreatic cancer and serology for viral hepatitis was negative. Laboratory evaluation of his stool revealed marked steatorrhoea. The LFTs continued to worsen with serum bilirubin rising to 24.2 mg/dl. At this point, biopsies of his liver as well as stomach and intestine were performed. All specimens stained positive with Congo-Red stain, consistent with a diagnosis of amyloidosis. Urine protein electrophoresis showed a faint kappa monoclonal peak and bone marrow biopsy showed increased plasma cells (7%) with kappa light chain restriction, consistent with the patient's amyloid. Chemotherapy was started and his immunosuppression was changed to mycophenolate moefetil and prednisone. He has completed three cycles of melphalan and dexamethasone with an excellent response so far, although the long term prognosis remains grim.

To the best of our knowledge, this is the first reported case of post transplant primary amyloidosis. In transplant patients presenting with unexplained GI symptoms, amyloidosis should be considered in the differential and appropriate work up should be undertaken.

THERE IS NO FREE LUNCH: THE NEGATIVE CONSEQUENCES OF TAKING CYCLOSPORINE WITH FOOD

Rodolfo Batarse, Linda Awdishu, Alex Dominguez, James Lane, Robert Steiner. UCSD Medical Center, San Diego, CA.USA. To prolong kidney allograft survival, transplant patients require adequate daily exposure to calcineurin inhibitors (CNI), as measured by area under the concentration time curve (AUC). Cyclosporine (CSA) absorption and overall drug exposure is reduced when taken with food. Pharmacokinetic (PK) modeling was used to examine the AUC effect of nonfasting CSA administration with a strict 12hour dosing interval versus fasting drug administration with a relaxed dosing interval. Changes in AUC with mixed dosing (AM dose fasting, and PM dose nonfasting) was also examined. Standard CNI PK parameters were employed. A population PK model on a data set of 500 patients was determined using nonlinear mixed effects modeling (NONMEM V.1) and Monte Carlo simulation. SAS9.2 was used to compare the AUCs. Model assumptions include a 30%reduction in bioavailability for the nonfasting state and CSA doses of 3.5mg/kg q12h for 7days. The CSA AUC0-24 for the fasting and nonfasting states were 3635mcg*hr/L, 2445mcg*hr/L, respectively. The CSA AUC0-24 with mixed dosing was 3090mcg*hr/L, with the AM C2 being 50% higher in the fasting state. The additional drug needed to overcome the decreased CNI absorption with food was 77316mg/yr, about $3402/year extra drug costs. In some patients, missing 20 fasting doses of CSA will give about the same AUC as perfect compliance with nonfasting CNI. In summary, always taking CNIs with food resulted in markedly lower overall exposure, a lower monthly AUC, equivalent to missing altogether 20 CNI doses/month. Published data indicate that CNI trough levels would not indicate the magnitude of underexposure, and reliable C2 would be impossible sans standardizing for food effects. Reinforcing adherence to fasting CNI dosing instead of a rigid 12hour dosing schedule will reduce the variability in CNI absorption, increase drug exposure, decrease pill burden and cost, and improve compliance. With once-a-day CNI dosing regimens, fasting dosing schedules will become even more important.

LACK OF BENEFIT FROM BUMETANIDE INFUSION AFTER CADAVERIC KIDNEY TRANSPLANTATION

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Post-ischemic acute tubular necrosis (ATN) is one of the most common causes of delayed graft function (DGF) after cadaveric kidney transplantation (CKTP). Use of diuretics in ATN is controversial. So far, there is no good evidence regarding diuretic use in post-op CKTP. This retrospective study examined the use of continuous bumetanide infusion to reduce DGF in CKTP.

We reviewed the charts of 97 patients who received kidney transplants from September 9, 2005 to August 30, 2006. Fifty-four out of 97 patients were included in the study. Thirty-one patients who received bumetanide infusion within 48 hours after surgery (group 1) were compared to 23 patients who did not receive bumetanide infusion (group 2) using Mann-Whitney test and regression analysis.

Twenty-five of 31 (80%) patients in group 1 required at least 1 dialysis in the first week postoperatively compared to only 4 of 23 (17%) in group 2, P=0.000. The number of dialyses (total 56 dialyses in 31 patients) was greater in group 1 than those in group 2 (total 9 dialyses in 4 patients), P=0.000. There was no advantage of bumetanide infusion and the average urine output was less in group 1 (median 49.16 vs. 110.81 cc/hour; P=0.0007). The serum creatinine was higher in group 1 at postoperative day 1 (median 8.3 vs. 6.9 mg/dl; P=0.02) and day 7 (median 5.4 vs. 1.9 mg/dl; P = 0.000). There was no difference between potassium levels at 1-week between 2 groups (median 4.2 vs. 4.3 mEq/L; P=0.3) and no difference in creatinine at 1 month after transplantation (median 1.6 vs. 1.6 mg/dl; P=0.61). There was no difference in cold or warm ischemia time, donor age, number of rejections, PTH and PRA between the 2 groups (P>0.05).

This study suggests that there may be no benefit of bumetanide infusion after CKTP for reducing DGF. Further prospective randomized controlled study may be needed.

CONCURRENT ACUTE RECURRENT RENAL ALLOGRAFT REJECTION, BK NEPHROPATHY/VIREMIA & OSMOTIC ACUTE RENAL FAILURE: A CASE REPORT

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Acute rejection of renal allograft and concurrent BK virus nephropathy (BKVN) poses diagnostic and therapeutic challenge. There is a consensus that endarterits, fibrinoid vascular necrosis and glomerulits (Banff II and III) should be regarded as evidence of concurrent rejection in the setting of BKVN/BKviremia. IVIG has been shown to be effective in acute rejection and in the treatment and prevention of viral infections in transplant patients. IVIG has been implicated in acute renal failure (ARF) with osmotic nephrosis. We report a rare case of concurrent acute recurrent cellular renal allograft rejection, BKVN/ viremia and IVIG related ARF.

A 62 y/o female underwent cadaveric kidney transplant on Jan 06 for ESRD from ADPKD. First rejection in Mar 06 treated with IV steroid & another acute IIB Banff rejection in May 06, treated with OKT3. She came back on Jul 21,06 with complaints of generalized weakness & mild fever of one day. Labs showed Bun 30, Cr 2.6, & her Cr 1.6 in Jun 21, 06. Renal biopsy done on Jul 25, 06 showed acute rejection Banff IIA. C4d and SV 40 stains negative. On Jul 28 Cr was 2.4, BKV PCR 29000 copies/ml, IVIG was started. Leflunomide was started on Jul 30. She became hypertensive with progressive decline in urine output(UO). Her Cr, osm gap & Na was 4.5, 20, 123 on Aug 2 and 7.5, 25 & 118 on Aug 4 respectively. Second biopsy on Aug 2 showed ATN with massive hydropic degeneration and resolving rejection. IVIG was stopped. Hemodialysis (HD) was done on Aug 4 &5. From Aug 5, Cr started to decline, UO improved, BP better controlled. On discharge, her Cr was 3, Na 136 & osm gap 4. BKVPCR was undetectable on Aug 23 & Sept 15 & Cr 1.8 & 2.1 on those dates; latest Cr 2.1on Nov27 06.

Treatment of concurrent acute rejection, BKVN seems feasible with reduction in immunosuppression, IVIG & leflunomide. More vigilance is required when IVIG is used in transplant cases. Osmotic ARF is quickly reversible with HD. Normalization of osm gap & pseudohyponatremia appears to indicate the adequate removal of osmolytes.

PSEUDO TRANSPLANT RENAL ARTERY STENOSIS AS A CAUSE OF RENAL IMPAIRMENT IN A PATIENT WITH KIDNEY TRANSPLANT

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Introduction: Most recipients of Renal Transplant experience progressive decline in kidney function over time after transplant. Common causes of chronic renal transplant dysfunction include chronic rejection, Hypertension, recurrent disease & cyclosporine nephrotoxicity.Transplant renal artery stenosis (TRAS) is a rare cause of chronic renal transplant dysfunction with an incidence of 1-2%. CASE: A 48 year old African American man with past medical history of Hypertension, Diabetes Mellitus, Peripheral Artery disease and status post Cadaveric Renal Transplant in 2002 presented with pneumonia and renal dysfunction. Patients Blood urea and nitrogen (BUN) and serum creatinine rose from his baseline of 30mg/dl & 2.1mg/dl to 57mg/dl & 3.4mg/dl respectively. Patient's renal function declined further over the next few days to BUN of 90 mg/dl & creatinine of 4.2mg/dl. Doppler ultrasound of the transplanted Kidney was normal.MRA of the pelvis showed significant Focal High grade stenosis in the Right external iliac Artery just proximal to the renal artery anastomosis. Transplant kidney biopsy revealed no evidence of acute rejection. A pelvic angiogram confirmed the above findings following which angioplasty was performed along the right external iliac artery. Patient responded with immediate diuresis and resolution of renal dysfunction to baseline within 48 hours.

Conclusion: Renal transplant Renovascular disease is a problematic but potentially correctable cause of chronic renal transplant dysfunction. It is important to identify and correct renal transplant renovascular disease, whether it is due to pseudo renal transplant artery stenosis or renal artery stenosis. Pseudo TRAS should be considered in the differential in patients with severe peripheral vascular disease. Percutaneous transluminal Angioplasty with or without stenting is an effective method of treatment in patients with renal transplant renovascular disease.

EARLY AND AGGRESSIVE RECURRENCE OF IDIOPATHIC MEMBRANOUS NEPHROPATHY IN A RENAL TRANSPLANT RECIPIENT

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Idiopathic Membranous Nephropathy (IMN) recurs in 10-30% of patients after transplantation. The mean onset time of recurrent disease is approximately 10-24 months post transplant. We report an early and aggressive recurrence within a few weeks post-transplant. Case: A 59 year old male, recipient of a pre-emptive living unrelated kidney for ESRD secondary to MGN, complained of 'frothy urine' 4 weeks following the transplantation, and increasing swelling of his legs. Examination showed edema, and labs revealed hypolbuminemia, hypercholesterolemia, and a normal S. Cr. Collection of 24 hour urine revealed 5 gm proteinuria. A renal biopsy was performed, showing minimal expansion of mesangial matrix on LM, immune-complex GN with pre-dominant IgG-C3-kappa-Lambda deposits in peripheral capillary walls on IF, and subepithelial deposits on EM, consistent with recurrent IMN. Secondary causes of MN were excluded (Hepatitis B and C, neoplasia, paraproteinemia). The patient was continued on his Tacrolimus, MMF and steroids, along with ACEI, ARBs and diuretics. Gradually, his serum albumin and edema worsened, with increasing need for diuretics. A repeat biopsy was done 6 months after transplant, which essentially showed the same picture of recurrent membranous GN on EM. Also, a perfusion scan showed no native perfusion or function, making native proteinuria very unlikely. It was decided to try a course of Rituximab, which was well tolerated. There was no response, and serum albumin and renal function began to decline, with repeat 24 hr proteinuria of 10 gm. Our patient presented far earlier then the reported mean time of onset with a much aggressive course. No risk factors for recurrence have been identified. The initial concerns with regards to the risk of recurrence with living related donors, presence of HLA-DR3 in the recipient, and aggressiveness of native disease have not been substantiated. Therapeutic interventions have been largely disappointing.

EXTENDED DOSING REGIMENS FOR INITIATION OF EPOETIN ALFA FOR TREATMENT OF ANEMIA OF CHRONIC KIDNEY DISEASE

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The objective of this open label, randomized, multicenter trial is to assess hemoglobin (Hb) response in non-dialysis subjects with anemia of CKD treated with one of 4 initiation regimens of epoetin alfa. Subjects were ≥18 years, had Hb <11 g/dL, GFR 15-90 mL/min/1.73 m^2, and had not received erythropoietic agents within 8 weeks (wks) prior to randomization. Subjects received: 10,000 Units (U) once weekly (QW), 20,000 U every 2 wks (Q2W), 20,000 U every 4 wks (Q4W) or 40,000 U Q4W of epoetin alfa SC for 16 wks. 127 subjects who received at least one dose of drug and completed or withdrew from the study were included in this pre-specified interim analysis. Mean age was 66.7±13.0 years; 43% were male; mean baseline GFR was 30.1±13.0 mL/min/1.73 m^2. Mean baseline Hb was similar across groups, ranging from 10.1±0.9 to 10.5±0.6 g/dL. Mean time on study was 15.6 wks for all subjects. Each subject's final Hb was the average of Hb values for the last 4 wks on study. All groups had an average final Hb of ≥11.0 g/dL: 11.9±0.5, 11.6±1.0, 11.0±1.1, and 11.5±0.9 g/dL in the QW, Q2W, 20,000 Q4W, and 40,000 Q4W groups, respectively. Adverse events were typical for this population. 17 subjects experienced at least one serious adverse event. 5 of these subjects had 7 serious cardiovascular events, 2 of which resulted in death (MI and CHF hospitalization, both in the 20,000 U Q2W arm). These interim results build upon previous data suggesting that epoetin alfa can be utilized using extended dosing regimens of QW, Q2W, or Q4W.

EFFICACY OF ERGOCALCIFEROL IN THE TREATMENT OF SECONDARY HYPERPARATHYROIDISM: RESULTS OF PROSPECTIVE, OPEN LABELED TRIAL IN PATIENTS WITH STAGE III CHRONIC KIDNEY DISEASE

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Introduction: Previous studies in patients with CKD, find that 80% of patients with GFR < 30 mls/min have 25OH cholecalciferol levels below 30 ng/ml. We speculated that oral supplementation of 25OH cholecalciferol could normalize 1,25-OH_2-Vit-D levels and reduce serum PTH levels in patients with stage III CKD.

To investigate this hypothesis, we performed a prospective open-labeled trial of 6 months of oral ergocalciferol (25OH vit D_2) (50,000 units) in 147 patients with stage III CKD. Patients were screened from a large out-patient CKD clinic and were considered for enrollment if 1) patients had a stable GFR (<40 ml/min); 2) 25OH vit D_2 less than 35 ng/ml; Of the enrolled patients, 58 completed 6 months of therapy and a documented 50% rise in (25OH vit D_2) levels. Stat-Signif:*=P<0.005; ^=P<0.0001

Table 1:

	GFR#1	VitD2#1	PTH#1	GFR#2	VitD2#2	PTH#2
Total	35+2.8	15+0.9	125+9	32+1.9	25+1.6	109±8.6
Non-Resp	30+2.7	12+1.4	90+11	27+2.8	30+3.4	118±15*
Respond	35+2.9	13+1.1	163+20*	32+3.3	30+2.5	89+12^

Results: PTH levels in the total population fell from 125±9 to 109±9 pg/ml, but this value did not reach statistical significance (P<0.08). Of the 58 patients, 27 (47%) failed to reduce PTH levels despite a significant (P<0.03) rise in 25OH-vit D_2 levels. In contrast, ergocalciferol decreased PTH levels among responders from 163±20 to 89±12 pg/ml (P<0.001). There were no differences in baseline GFR or 25OH-vit D_2 among responsive and non-responsive patients, but basal PTH levels were significantly (P<0.03) higher among the responsive group. In conclusion, 6 months of oral supplementation with ergocalciferol decreased PTH levels in over 50% patients with stage III CKD. The increased number of patients with undetectable levels of 5OH-vit-D2 suggests that higher doses may required to reverse secondary hyperparathyroidism.

LEFT VENTRICULAR DYSFUNCTION IS ASSOCIATED WITH IRON DEFICIENCY IN RATS WITH EXPERIMENTAL CKD.

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Anemia and left ventricular (LV) hypertrophy, which is an independent variable for developing congestive heart failure, are both increased in prevalence in patients with chronic kidney disease (CKD). In this study we evaluated the relationship between LV function and iron status in rats with CKD, using the 5/6subtotal-nephrectomy (STNx) model. Male Sprague Dawley rats in two groups, G1: 5/6subtotal-nephrectomy (STNx), G2: sham-operation. Cr. clearance (Cr.cl), hemoglobin (Hb), serum iron (SI), fractional shortening ($FS_{\%}$) by echocardiogram were evaluated. Six months after STNx, heart and kidney were processed by immunohistochemistry with antibodies against erythropoietin (EPO), ferritin and hypoxia inducible factor-1α (HIF-1α). At 6 months post-surgery: Hb(g/dl) G1: 10.8±0.8, G2: 14.7±0.6 ($p<.01$); SI (μg/dl) G1: 154.5±24.5, G2: 287.5±32.1 ($p<.01$); TSAT(%) G1: 16.2±3.7, G2: 36.5±3.9 ($p<.01$); Cr.cl (ml/min/bw) G1: 1.3 ±0.1, G2: 4.2±0.1 ($p<.01$); Heart weight (g) G1: 2.2±0.1, G2: 1.1±0.1 ($p<.01$); $FS_{\%}$ G1: 28.4±2.5, G2: 45.1±4.1 ($p <.01$). There was a positive correlation between Hb and $FS_{\%}$ ($r=0.95$, $p<.01$) and between SI and $FS_{\%}$ ($r=0.86$, $p<.01$) in the STNx group. Immunohistochemistry (% positive staining area): 1)EPO in kidney G1: 10.2±1.4, G2: 1.2±0.6 ($p<.01$); 2)EPO in heart G1: 2.6±0.4, G2: 0.8±0.2 ($p<.01$); 3)Ferritin in kidney: G1: 1.0±0.5, G2: 2.5±0.5 ($p<.01$); 4)Ferritin in heart: G1: 0.8±0.4, G2: 1.9±0.3 ($p<.01$); 5)HIF-1α (positive cells/area) in kidney G1: 70±16, G2: 10±3 ($p<.01$), in heart G1: 32±5, G2: 4±1 ($p<.01$). In STNx group, there was a negative correlation between: 6) Hb and HIF-1α in heart ($r=-0.96$, $p<.01$), 7)SI and HIF-1α in heart ($r=-0.87$, $p<.01$). Similar relations were also observed in kidney in the STNx group. These data suggest that iron deposits are reduced in rats with CKD by STNx. EPO was overexpressed not only in kidney but also in heart; however, these animals present an insufficient EPO response related to the anemic status. LV systolic dysfunction was associated with iron deficiency.

PLASMAPHERESIS IN NEUROMYELITIS OPTICA (NMO)

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A twenty-seven year old female with a history of transverse myelitis treated with corticosteroids presented with lower extremity parasthesia and urinary retention for two days. She was given intravenous steroids but her clinical condition worsened until she was unable to stand. Pertinent studies included a negative lumbar puncture, spinal MRI showing multi-level spinal cord enhancement, and positive serum IgG autoantibody (NMO-IgG). Given these findings, plasmapheresis was initiated with dramatic improvement and she was discharged after five plasma exchanges. As an outpatient she had two more sessions of plasmapheresis and was started on azathioprine.

Neuromyelitis optica (NMO) is an idiopathic, demyelinating syndrome of the central nervous system characterized by episodes of optic neuritis and myelitis. The diagnostic criteria include optic neuritis, transverse myelitis and two of the following: sero-positive NMO-IgG, contiguous spinal cord levels with increased MRI signal over three or more vertebra, and a brain MRI not diagnostic for multiple sclerosis. Studies involving plasmapheresis versus sham exchanges have shown that plasmapheresis is beneficial in exacerbations of demyelinating diseases like NMO. In 2004 NMO-IgG was the first serum autoantibody biomarker discovered in a demyelinating inflammatory disorder, providing further evidence that a humoral pathomechanism is most likely responsible for NMO and that plasmapheresis can be an effective option in steroid refractory cases of CNS demyelination.

Physicians should be aware of the importance of plasmapheresis in demyelinating disorders and its crucial role in cases refractory to corticosteroid treatment.

LIMITATIONS OF SODIUM HYPOCHLORITE AS A DISINFECTANT

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Sodium hypochlorite, the active agent in bleach solutions, has been a trusted disinfectant for decades. Recently the literature indicates that this well-known and inexpensive chemical has some serious limits as a surface disinfectant. Hypochlorite has been demonstrated to be ineffective in eliminating some infectious agents, like *Staphylococcus aureus*, at concentrations used in health care practice and under conditions of organic load, such as blood. There are also serious chemical compatibility concerns with respect to wipe material interactions with bleach solutions. Laboratory testing has demonstrated a 75% degradation of active ingredient in a solution starting ~6900 ppm (~10% commercial bleach) contaminated with 0.2% bovine serum albumin in 5 hours. Further testing resulted in a 50% reduction in hypochlorite concentration for a solution starting at ~670 ppm (~1% commercial bleach) contaminated with 0.08% whole bovine blood in 5 hours. Concurrent testing revealed a surprising effect of wipe material on freshly prepared dilute bleach solutions. Paper-based towels degraded as much as 80% of the hypochlorite concentration in less than 1 minute of contact. Material mixtures containing cellulose degraded 25-60% of the active ingredient in the same time frame.

These results indicate a need in the hospital community to seriously examine the limits of a commonly used disinfectant and consider options that may be less susceptible to these limits.

DISEASE KNOWLEDGE AND UNMET PATIENT EDUCATION NEEDS AMONG EPOETIN RECIPIENTS ON HEMODIALYSIS (HD): PATIENT SURVEY WITHIN A TIME AND MOTION STUDY

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The current standard of HD care in the US is challenged by increasing numbers of patients with CKD and a stagnant number of caretakers. The introduction of C.E.R.A., of a once-monthly continuous erythropoietin receptor activator promises to benefit this situation. In a survey conducted during a multicenter time and motion study we evaluated knowledge and education needs among HD patients about their disease including anemia. Patients rated their knowledge of 6 aspects of CKD. They also rated the importance of 8 potential additional areas of care or education (advice on dealing with fatigue, information about easing CKD symptoms, discussion of patients' health problems, general information about CKD, dietary advice, information about anemia, information about transplants, and advice on self-care/home dialysis). Among 444 patients from 5 participating centers, 91 completed the survey. The majority of patients (77% and 76%, respectively) felt that they did not have sufficient information on the important topics of how CKD causes anemia and the symptoms of anemia. Advice on dealing with fatigue and information about easing symptoms of CKD were the additional needs most desired by patients if healthcare professionals had additional time available. These results suggest that substantial gaps exist in educating and guiding HD patients. Once monthly C.E.R.A. administration may free time for caretakers thereby providing the opportunity for more patient care and education.

ACTIVITY-BASED COST ANALYSIS OF IN-CENTER ANEMIA TREATMENT IN HEMODIALYSIS PATIENTS

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The cost of managing anemia of chronic kidney disease is not limited to the cost of drug acquisition but also includes the cost of the necessary labor. This multicenter activity-based costing study evaluated the time and costs attributable to epoetin (EPO) treatment of dialysis patients three times/wk in 5 centers in the USA. It also modeled the potential time and cost savings with C.E.R.A., a novel continuous erythropoietin receptor activator that is effective when administered at once-monthly intervals. At each center, time and motion data were gathered by trained observers using chronometers to determine time spent on pre-identified anemia management tasks. Healthcare personnel were also interviewed to obtain information on unobserved and infrequent tasks. Labor costs were calculated from wage and benefit rates in year 2006 dollars. Usage levels and costs for non-drug supplies were determined. Total time (observed and reported tasks) per patient per year expended on anemia management averaged 608 min (95% CI: 471,747 min) for EPO, with an average annualized cost per patient of $548 (95% CI: $464, $633). In contrast, for C.E.R.A. (modeled at 100% uptake, i.e., if all patients used C.E.R.A.), annual average time expenditure per patient decreased by 79% (127 min [95%CI: 87,166 min]), and annualized costs per patient reduced by 81% ($104 [95% CI: $76, $132]), compared with EPO. In conclusion, once-monthly C.E.R.A. may improve the management of renal anemia compared with current management practice.

ORAL FISH OIL SUPPLEMENTATION IS EFFICACIOUS IN CHRONIC HEMODIALYSIS PATIENTS: A PILOT STUDY

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Hemodialysis patients may obtain clinical benefit from supplementation with the fish oil-derived long chain omega-3 polyunsaturated fatty acids (n-3 PUFAs) eicosapentaenoic(EPA, 20:5n-3) and docosahexaenoic (DHA, 22:6n-3) acids, particularly given our previous observations that this population consumes inadequate dietary fish and has suboptimal red blood cell (RBC) n-3 PUFA levels. Most fish oil supplementation studies in dialysis patients have been non-randomized, used supraphysiological n-3 PUFA doses, and did not document the dose-response relationship and/or measure the most clinically relevant fatty acid fractions. We tested the hypothesis that supplementing hemodialysis patients over 12 weeks with more modest doses (approximately 1 gm fish oil daily, the recommended American Heart Association dose) would be efficacious in boosting red blood cell fatty acid levels by performing a randomized, placebo-controlled, double-blinded study in an urban American hemodialysis population. Twelve subjects were randomized to 1.3 g fish oil or placebo (corn/soybean oil) in a 2:1 ratio (i.e. 8:4). 75% of subjects consumed one or less fish servings a week. Baseline EPA and DHA RBC levels were relatively low at (mean ± SD) 3.2 ± 2.2 and 0.29 ± 0.24, respectively. Post-supplementation EPA and DHA RBC levels were dramatically increased in the fish oil group [% EPA change (fish oil vs placebo): +395 vs -27, p=0.004; % DHA change: +160 vs -27, p=0.008]. Four subjects in the fish oil group noted minor, primarily gastrointestinal, side effects. These findings suggest that supplementation of hemodialysis patients with even modest doses of fish oil dramatically boosts RBC n-3 PUFA content and is generally well-tolerated. Larger studies will need to confirm these findings and determine whether supplementation improves clinical outcomes.

HISTOMORPHOLOGIC BONE ALTERATIONS IN CKD - CORRELATION WITH BIOCHEMICAL PARAMETERS

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Renal osteodystrophy is best diagnosed by invasive bone biopsy. The objective of the present study is to establish the spectrum of bone disease by histomorphometric analysis, and to determine the correlation between biochemical and histomorphometric parameters.

45 CKD patients (25-dialysis, 20-non-dialysis) were investigated. Dialysis patients received 8-12 hours of dialysis/week where aluminum concentration of dialysate was <10µg/L. All participants were on non-aluminum phosphate binders and oral calcitriol (0.25-1.0µg/d). Serum calcium, phosphate, alkaline phosphatase (ALP), intact parathyroid hormone (iPTH) levels were measured; radiological survey & bone biopsy (mod Jamshidi needle- ant iliac crest) were performed on each participant. Histomorphometric parameters like percent osteoid, bone osteoblast and osteoclast interface, peritrabecular and endosteal fibrosis were calculated and type of uremic bone disease according to criteria set by Sherrard et al 1993 was determined. Statistical analysis using chi-square, paired t-test, and linear regression analysis was done.

Bone histology revealed hyperparathyroid bone disease (HPBD) in 23, mixed uremic osteodystrophy (MUO) in 14, mild disease in 4, osteomalacia in 3, and aplastic bone disease (ABD) only in 1 patient. HPBD was the predominant histological type (50%), and was commoner in dialysis patients (60%). MUO instead was the most common type in pre-dialysis group (50%). Clinical symptoms, radiological findings, calcium and phosphorous levels ($p=0.085$ and $p=0.90$) had no correlation with type of bone disease. ALP and iPTH correlated with histological subtypes ($p=0.002$ for both) with highest values being in HPBD and lowest in ABD. iPTH correlated significantly with osteoclast interface (corr. coeff=0.72), osteoblast interface and %fibrosis (corr. coeff=0.60) suggesting high turnover, but not with mineralization or percentage of osteoid.

Although ALP and iPTH are good indicators of bone turnover, biopsy is required to determine exact histological type. Diagnosis of aluminum and ABD can be established only on histological examination.

COST-EFFECTIVENESS OF TREATING PATIENTS WITH CINACALCET EARLY VERSUS DELAYING TREATMENT WITH CINACALCET FOR SECONDARY HYPERPARATHYROIDISM IN PATIENTS WITH ESRD.

Ray, J[1]; Borker, R[2]; Barber, B[2]; Valentine, W[1]; Belozeroff, V[2]; Palmer, A[1].
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The objective of this research was to estimate lifetime cost-effectiveness of treating patients with cinacalcet early (when parathyroid hormone (PTH) levels are in the range of 300-500 pg/mL) versus delaying treatment with cinacalcet (cinacalcet initiated when PTH levels are >800 pg/mL) in patients with secondary hyperparathyroidism (SHPT) in the US setting. A Markov model was developed to simulate the effects of early versus delayed use of cinacalcet (plus standard of care). Four different PTH ranges (≤ 300 pg/mL; 301 – 500 pg/mL; 501 -800 pg/mL; > 800 pg/mL) were used to represent 4 different health states within the Markov model. Associated with each Markov state (PTH range) were varying risks of major SHPT complications, including cardiovascular disease (CVD), fracture (Fx) and parathyroidectomy (PTx). Baseline cohort characteristics and risks of CVD, Fx and PTx by PTH category were derived from a large dialysis database and published sources. Costs were estimated from the USRDS database and reported in 2004 US Dollars ($). Clinical and economic outcomes were discounted at 3.0% *per annum*. Early treatment was projected to improve quality-adjusted life years (QALYs) by 0.41 years compared to delaying treatment. The incremental cost-effectiveness ratio was $21,375 per QALY gained. Early treatment with cinacalcet was associated with improvements in QALYs and would represent good value for money compared to delaying treatment with cinacalcet.

ADRENAL INSUFFICIENCY DUE TO MEGESTROL WITHDRAWAL IN A PATIENT ON HEMODIALYSIS

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Megestrol is a progestational steroid that is used for the management of breast and endometrial carcinoma, and AIDS related cachexia and wasting. Megestrol is frequently used as an appetite stimulant in dialysis patients with anorexia. It has glucocorticoid-like activity and suppresses the hypothalamus-pituitary-axis (HPA). There have been case reports of adrenal insufficiency with the use or withdrawal of megestrol in AIDS and cancer patients, but none as far as we know, in hemodialysis patients.

A 65 year old Caucasian female with past medical history of end stage renal disease on hemodialysis, cirrhosis, atrial fibrillation, and GERD presented with complaints of progressively worsening generalized weakness, nausea, and vomiting over the course of preceding 2 weeks. Her medication history was significant for the use of megestrol as an appetite stimulant for about 2 years that had been discontinued 3 weeks prior to her arrival, when she was diagnosed to have portal vein thrombosis. On the present hospital admission she was also found to be hypotensive, with a BP of 80/40 mm Hg. She was admitted to the ICU and managed with IV fluids, vasopressors, and dexamethasone. A cosyntropin stimulation test was subsequently performed the following morning, which confirmed that she had adrenal insufficiency (Baseline-3.6 mcg/dl, 30 min-9.5 mcg/dl, 60 min-12.6 mcg/dl). Her blood pressure improved with these interventions and within 6 hours, she was weaned off vasopressors and her BP normalized. Following this, she was kept on maintenance dose of steroids. No other cause of hypotension was identified. Another cosyntropin stimulation test is planned in 3 months.

This case highlights the effects of megestrol on HPA axis suppression, and adrenal insufficiency after megestrol withdrawal. Though rare, it is prudent for nephrologists using megestrol as an appetite stimulant to be aware of this life threatening complication with the use of megestrol, and one should have a high index of suspicion of adrenal insufficiency in patients who are on megestrol or in whom it has been recently stopped.

WHOLE BLOOD ACCUMULATION OF ASYMMETRIC DIMETHYLARGININE IN END-STAGE RENAL DISEASE

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Plasma asymmetric dimethylarginine (ADMA) is significantly elevated in patients with renal disease and associated with cardiovascular mortality. Our recent study with a rodent model indicates that whole blood (WB) possesses large concentrations of protein-incorporated ADMA and the proteolytic machinery necessary for its release. To explore the link between WB and plasma ADMA in humans, we compared plasma ADMA and ex vivo ADMA accumulation in blood from subjects with and without end stage renal disease (ESRD). Pre-dialysis blood samples were obtained from 13 ESRD patients receiving chronic outpatient hemodialysis and 13 subjects without kidney disease who were matched for age, gender, race and presence of diabetes and/or hypertension. ADMA plasma concentrations were measured at baseline and ADMA levels from WB supernatant (WBSUP, e.g. the soluble fraction of lysed blood) were quantified over a 5h ex vivo incubation. ADMA was measured by high-pressure liquid chromatography. Baseline values were compared using unpaired two sided t-tests. The slopes derived from ADMA accumulation in WBSUP incubations were analyzed with a marginal effects linear regression model. ESRD patients had higher plasma ADMA than matched controls (0.83±0.05 vs. 0.61±0.06 μM, p=0.05, respectively). Ex vivo incubation of WBSUP showed a significant accumulation of ADMA in both groups. However, the ESRD population had a 47% greater rate of accumulation than matched controls (p=0.04). These findings confirm our animal data and further support a role for whole blood as a potential source for pathophysiologic elevations of free plasma ADMA.

RELAXATION THERAPY IN THE NEPHROLOGY SETTING: IMPLICATIONS FOR PRACTICE

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This study examined the effectiveness of relaxation techniques with patients of a regional hospital-based Nephrology Program using a qualitative methodology. The initial sample consisted of twenty-five participants of all treatment modalities. Respondents were asked to complete a survey. All participants finished one to five relaxation therapy sessions over a 6-month duration. Relaxation techniques consisted of progressive muscle relaxation, deep breathing, guided imagery and refocusing. One year later a random sample of twenty-one participants were surveyed to measure if relaxation skills (a) were continuing to be utilized, (b) continued to be effective, (c) were useful to justify recommendation.

Results suggest that the patients were overwhelmingly pleased with relaxation as an effective technique to assist with amelioration of caregiver stress, anxiety, sleep disturbance, fear of needles, difficulty coping, fear of dialysis and pain control. One year later, 90.5% of respondents are continuing to practice the relaxation skills taught to them. 100% of the respondents indicated that they would recommend this therapy to others. Implications for practice might include Relaxation Therapy as a complementary tool to assist patients during invasive surgical interventions.

COMBINATION THERAPY INCLUDING SEVELAMER HCL TO CONTROL SERUM CHOLESTEROL AND TRIGLYCERIDE LEVELS. Judy Pata, Stephen Silver, Rochester General Hospital Dialysis Center Rochester, NY USA

Hyperlipidemia can be difficult to control in the dialysis patient when statins are not an option.

A 79 year old, non-diabetic female with stage 5 CKD, started CAPD on 6/1/04 and APD on 7/21/04. This active individual is adherent with medication and diet (3 gm Na, heart healthy, high protein, low phosphorus.) Weight for height is within normal limits and albumins are within normal. The patient had elevated total cholesterol, triglycerides, and LDL cholesterol. Four different statins had been prescribed but none were tolerated due to muscle pain. Ezetimibe was tolerated at a dose of 10 mg daily but lipid levels remained elevated. A combination of non-statin therapies was then instituted. Laboratory values (all units in mg/dl.) and medications are noted below:

Date	Chol	TG	LDL	HDL	P	Medications
1/04	252	325	147	40	5.5	ezetimibe 10 mg/d
6/04	207	328	103	38	4.9	Addition: niacin tapering up to 1000 mg/d
11/04	248	299	136	52	4.6	1/29/04 niacin discontinued - rash
2/05	254	512		41	4.4	
10/05	244	497			4.6	Addition: fish oil 2000 mg bid
1/06	273	389	133	62	5.4	
3/06					5.2	Addition: sevelamer 1600 mg tid
7/06	195	271	96	45	5.9	
11/06	190	305	86	43	5.6	fish oil 2000 mg bid ezetimibe 10 mg/d sevelamer 1600 mg tid

With the introduction of fish oil in October 2005, the triglyceride level dropped in January 2006. The HDL cholesterol was also improved but LDL cholesterol remained elevated. Sevelamer was substituted for calcium carbonate phosphate binder in March 2006. The July and November 2006 draws demonstrated an improvement in total cholesterol, LDL and triglyceride levels compared to January. The previous improvement in the HDL levels was not sustained.

In conclusion, addition of sevelamer to the patient's lipid lowering regimen may have resulted in further lowering of triglycerides as well as LDL.

DOSING INTERVALS AND HEMOGLOBIN CONTROL IN PATIENTS WITH ANEMIA OF CHRONIC KIDNEY DISEASE TREATED WITH ERYTHROPOIESIS STIMULATING AGENTS

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Many clinicians see a need to extend dosing intervals of current erythropoiesis stimulating agents (ESAs) beyond the approved intervals. Thus, the effects of extended intervals on hemoglobin (Hb) control in real-world practice merit further study. This retrospective chart review study examined anemia management patterns and Hb outcomes in adult outpatients treated for anemia of CKD not on dialysis at a tertiary CKD clinic. Patients receiving ESAs between Jan. 1, 2000 and Mar. 1, 2005 were eligible for the study. Those who underwent dialysis or transplantation were censored as well as those who died. Twenty-one patients received only epoetin (EPO), and seventy-four patients received only darbepoetin (DA). Sixteen patients switched from one agent to the other and were excluded from further analysis. Initial, dominant, and final dosing intervals were determined from chart review. Control of Hb was assessed by the magnitude and total duration of deviations from target range (11-12 g/dL) and the percentage of Hb measurements below, within, and above target range. All EPO patients began therapy weekly and all DA patients began at Q2W. Many attempted extended dominant intervals (Q2W in 62% of EPO patients and Q3W in 53% of DA patients). However, 80% of EPO patients with Q2W dominant intervals returned to Q1W. Similarly, 63% of DA patients with Q3W dominant intervals had final intervals of Q2W. Patients receiving EPO at Q2W or DA at Q3W had 31% and 46% of Hb measurements greater than 12 g/dL and 44% and 36% of Hb measurements of less than 11 g/dL. Many patients at this center were tried on extended intervals with current agents but were returned to more frequent intervals, possibly due to unsustainable Hb control at extended intervals.

COMPARISON OF EMPLOYER COST AMONG EMPLOYEES WITH ANEMIA OF CHRONIC KIDNEY DISEASE, HEALTHY EMPLOYEES, AND THOSE WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE OR RHEUMATOID ARTHRITIS

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Despite the debilitating nature of anemia of CKD, few studies have estimated its cost to employers or compared those costs to other common chronic conditions. This analysis compared the employer cost burden for employees of a major U.S. manufacturer who had either anemia of CKD, were healthy, or had COPD or RA. Data were reported for a span of 15 months and mean direct and indirect costs were calculated for each cohort. Direct costs included medical and pharmacy costs, while indirect costs included absenteeism (work days lost) and presenteeism (decrease in productivity during work time due to illness). Presenteeism was measured by SKU (stock keeping units), a numeric identifier used in tracking parts and specific product inventory. This number is used as a proxy for productivity in settings where employees install the relevant SKU. Independent t-tests were conducted to identify significant cost differences between cohorts and a linear regression was used to determine the effect of each disease on cost. Anemia of CKD was shown to have a significant impact on direct and indirect costs. Healthy employees and employees with COPD or RA had 38.1-60.0% lower pharmacy costs than those with anemia of CKD. Healthy employees' medical costs were 78.1% lower than the anemic-CKD cohort's costs, however, medical costs were similar between patients with anemia of CKD and RA or COPD. Healthy employees and those with RA or COPD were more productive than those with anemia of CKD; working 29.6-73.5% more days and producing 57.3-107.7% more SKU. These findings indicate that anemia of CKD resulted in more work days lost, lower productivity levels and higher healthcare costs per patient than COPD or RA.

DRUG UTILIZATION AND COST CONSIDERATIONS OF ERYTHROPOIETIC STIMULATING AGENTS IN CHRONIC KIDNEY DISEASE PATIENTS NOT RECEIVING DIALYSIS

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This analysis aimed to examine recent epoetin alfa (EPO) and darbepoetin alfa (DARB) treatment patterns and corresponding drug costs in CKD patients not receiving dialysis.

A medical claims analysis was conducted from 1/2004 through 12/2005 using the PharMetrics Patient-Centric database. Patients included in the study were ≥18 years, had ≥1 claim for CKD, and were newly initiated on EPO or DARB and received ≥2 doses. Patients diagnosed with cancer or receiving chemotherapy were excluded. The weighted mean weekly dose was scaled based on the duration of therapy. September 2006 wholesale acquisition costs were used to calculate drug costs (EPO $12.17/1,000 Units; DARB $4.446/mcg).

The study population consisted of 187 patients who received EPO and 129 who received DARB. EPO patients were significantly older (mean age: EPO 59 years, DARB 53 years, $p<.05$). The proportion of women was similar between the two groups (EPO: 55%; DARB: 49%). Extended dosing frequency (defined as every 2 weeks or greater, ≥Q2W) during treatment was observed in the majority of patients in both groups (EPO – QW: 39%, Q2W: 47%, Q3W: 8%, ≥Q4W: 6%; DARB – QW: 10%, Q2W: 53%, Q3W: 19%, ≥Q4W: 18%). The weighted mean weekly dose was 13,563 ± 10,245 Units for EPO and 55 ± 36 mcg for DARB. Based on these doses, mean weekly drug cost was 48% higher in the DARB group (EPO $165; DARB $245; $p<.0001$).

These findings, based on actual clinical practice, are similar to those reported in previously published observational studies.

IRON-MAGNESIUM HYDROXYCARBONATE (ALPHAREN): A NOVEL NON CALCIUM CONTAINING PHOSPHATE BINDER FOR THE TREATMENT OF HYPERPHOSPHATAEMIA IN CHRONIC HAEMODIALYSIS PATIENTS.

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A key therapeutic aim in the management of chronic haemodialysis (HD) patients on dialysis is the control of serum phosphate. Current recommendations limit the use of calcium-containing binders. Alpharen is a mixed metal (iron and magnesium) hydroxycarbonate. The ions are held in an insoluble hydrotalcite structure and acts by exchange of its carbonate groups with intestinal free phosphate. The aim of this first patient study was to test the preliminary efficacy and tolerability of Iron Magnesium Hydroxycarbonate in the management of hyperphosphataemia in HD patients.

The study was a randomised, double blind comparison of placebo to two doses of Iron Magnesium Hydroxycarbonate (1 g t..i.d. or 2 g t..i.d.). Patients underwent initial washout of their current phosphate binder treatment for 2-4 weeks after which, Iron Magnesium Hydroxycarbonate was administered just prior to meals for 21 days. Vitamin D therapy was maintained without dose change over the study period.

Sixty three patients (21 per arm) entered the treatment phase. In the intention to treat analysis, mean serum phosphate prior to washout was 4.75 mg/dl and rose to 6.69 mg/dl during washout. Iron Magnesium Hydroxycarbonate (1 g t.i.d.) was associated with significant reduction in mean serum phosphate to 5.32 mg/dl (ANCOVA model $p<0.05$). The adverse event profile for the 1g and placebo arms were similar. Iron Magnesium Hydroxycarbonate at a dose of 2g t.i.d. resulted in a significant reduction of serum phosphate (mean 4.55 mg/dl, $p<0.05$). This dose was associated with GIT-related adverse events in over half the patients. Iron Magnesium Hydroxycarbonate treatment was not associated with either transient or sustained hypercalcaemia. There was no detected change in any measured indices of iron status. Both 1 and 2 g doses were associated with a statistically significant elevation of serum magnesium levels although no serious adverse events were attributable to hypermagnesaemia.

Iron Magnesium Hydroxycarbonate is an effective and well tolerated treatment for hyperphosphataemia in chronic HD patients. Further investigation is underway to define the optimal dosing schedule and long-term safety and efficacy.

THE NUTRITION PHYSICAL EXAMINATION IN KIDNEY TRANSPLANT EVALUATIONS

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The nutrition physical examination (NPE) is a valuable nutrition assessment tool for experienced practitioners. Given nutrient losses with chronic renal replacement therapy, as well as polypharmacy common in chronic kidney disease (CKD), those who present for a kidney transplant evaluation are high risk for nutrient depletion that may lead to positive findings in the NPE.

An organized approach to the exam, with good lighting and helpful tools such as an illuminated magnifying glass, are important. Recognizing normal and abnormal findings in an NPE takes considerable practice. Kelly has presented many professional workshops on the NPE for renal dietitians and has published helpful peer-reviewed articles which include valuable color photographs to describe lesions seen in an urban hemodialysis practice.

The author has included the NPE in pre-kidney transplant nutrition evaluations for 2 years. In one case a female with a previous surgical history including a jejuno-ileal bypass in 1972 presented with sparse hair and Beau's lines on the fingernails. Serum zinc suggested a zinc deficiency and repletion was recommended. NPE findings, in combination with knowledge of drug-nutrient interactions and the pathophysiology of the patient's medical and surgical history, lead to helpful interventions that might otherwise not have been considered.

The NPE strengthens the integrity of the Nutrition Care Process in the care of CKD patients.

PLASMA REFERENCE STANDARDS FOR PTH ASSAYS IN PATIENTS ON HEMODIALYSIS

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Measurement of plasma PTH concentration is critical for the evaluation and treatment of Mineral and Bone Disorder in CKD (CKD-MBD). The KDOQI Guidelines suggest PTH target ranges and, in turn, clinical treatment protocols are based on these targets. However, the evidence used to support these target ranges was primarily based on an assay for “Intact PTH” that is no longer used. In practice, there are up to 15 different Intact PTH assays in use worldwide. These assays may provide disparate results due to varying cross reactivity with PTH fragments that accumulate in CKD patients and other factors. This pilot study is to test the feasibility of developing biologic reference standards for PTH that can be used to estimate the variation between the different PTH assays. This method of ongoing analysis of PTH assays would help interpretation of clinical results to guide treatment and allow for comparison of research studies in CKD-MBD. Plasma was obtained from hemodialysis patients with varying degrees of SHPT. The specimens were acquired using plasmapheresis. The citrated plasma was then aliquoted into vials and lyophilized for distribution. Eight labs in the U.S. were asked to participate in the pilot test and to analyze four samples for PTH using whatever "Intact" PTH assay they have available. Values obtained, in pg/mL, ranged from 565-1054; 407-686; 565-741; and 376-683 in Samples 1-4, respectively. These data show that, as expected, there is some variation in results for the same sample between different labs and assays. Strict adherence to numerical values for PTH ranges in current practice guidelines is not advisable.

LANTHANUM CARBONATE VS STANDARD PHOSPHATE BINDER THERAPY: EVOLUTION OF RENAL OSTEODYSTROPHY OVER 1 AND 2 YEARS OF TREATMENT

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Lanthanum carbonate (LC, Fosrenol®) and standard phosphate binder (Stx, primarily calcium-based agents) therapies were compared in a prospective, randomized controlled trial, designed to investigate the evolution of renal osteodystrophy over 2 years of treatment.

Following tetracycline labelling, bone biopsies were taken from hemodialysis patients before randomization and following 1 and/or 2 years of treatment. Bone turnover, activation frequency, bone volume and mineralization status (mineralization lag time [Mlt] and osteoid thickness [O.th]) were evaluated.

Baseline demographics were similar between the treatment groups. Paired biopsies were available from 99 patients: 1-year biopsies from 34 patients receiving Stx and 32 receiving LC, and 2-year biopsies from 24 patients receiving Stx and 32 receiving LC.

Mean serum phosphorus levels decreased in both treatment groups; values remained below the 5.9 mg/dl target for the duration of the study. In patients receiving LC, serum calcium levels were lower, and PTH, osteocalcin and bone specific alkaline phosphatase levels were higher, compared with Stx treatment.

Group comparisons of histomorphometric bone parameters with Stx and LC showed no statistical differences in mean values after 1 or 2 years of treatment. Analysis of changes in individual patients with respect to normal ranges showed improvements in bone turnover and formation at 2 years with LC, compared with Stx treatment. Two patients in the LC group developed a mineralization defect (Mlt > 100 days and O.th > 20 μm) compared with no patients in the Stx group.

In conclusion, LC treatment resulted in similar serum phosphorus control, lower serum calcium levels, and biochemical and histological evidence of increased bone formation, compared with Stx.

ANEMIA TREATMENT PATTERNS IN CHRONIC KIDNEY DISEASE IN PRE-DIALYSIS PATIENTS USING DARBEPOETIN ALFA (NESP)

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With recent advances in chronic kidney disease (CKD) anemia therapy, providers now look to extend dose intervals of erythropoiesis stimulating agents (ESA). We conducted a retrospective study of electronic medical records from the Kidney Specialists of Minnesota, which has a protocol to extend patient ESA dosing to monthly intervals.

Eligible patients had pre-dialysis CKD at the start of NESP treatment and at least 6 months follow-up. NESP dosing was evaluated for initial and dominant intervals of every 2 weeks (Q2W), 4-6 weeks (Q4W), and no dominant interval (NDI).

Of the 435 eligible patients, 58% were female, the mean age was 70 years (with 69% age 65+); 17% of patients were CKD stage 3, 48% were stage 4, and 35% were stage 5a. More than half (54%) of patients began NESP at interval of Q2W and 21% began on Q4W schedule. The dominant intervals observed were Q2W for 20% of patients, Q4W for 52%, and NDI for 23%. The mean initial dose for patients with Q2W dominant interval was 38% higher than Q4W patients (43.1mcg/week vs. 31.3mcg/week). The mean final dose observed was 43% higher for Q2W (50.2 mcg/week vs. 35.2 mcg/week) and the mean dominant dose was 164% higher for Q2W patients vs. Q4W (60.4 mcg/week vs. 22.9 mcg/week).

Although providers have been looking to extend ESA dosing intervals, this clinic experience shows it works in only half of all patients and those with lower dose requirements. Patients whose dominant dosing interval was Q4W required substantially less NESP than those on Q2W.

ONCE-WEEKLY (QW) DARBEPOETIN ALFA ADMINISTRATION IN ERYTHROPOIESIS-STIMULATING PROTEIN (ESP)-NAÏVE PATIENTS WITH CHRONIC KIDNEY DISEASE (CKD): HEMOGLOBIN (HB) LEVELS WITHIN THE FIRST 8 WEEKS OF THERAPY

Reshma Kewalramani, Chao-Yin Chen, and Preston Klassen. Amgen Inc., Thousand Oaks, CA, USA.

Darbepoetin alfa is an ESP that can be administered at a variety of intervals to achieve and maintain Hb levels in study patients with CKD not receiving dialysis. The analysis presented here was conducted to assess Hb levels during the first 8 weeks of subcutaneous QW darbepoetin alfa therapy in ESP-naïve CKD patients. The primary analysis has been published previously (Locatelli et al, *Kidney Int*, 2001).

Patients were enrolled if they were ≥18 years of age, had Hb levels <11 g/dL, had CrCl <30 mL/min but were not receiving dialysis, and were iron replete. Subjects initiated QW darbepoetin alfa at 0.45 mcg/kg, with subsequent doses titrated to achieve a Hb level between 11 and 13 g/dL. The primary endpoint was the proportion of subjects who achieved at least one Hb measurement ≥1 g/dL from baseline and ≥11 g/dL during the first 24 weeks of therapy.

Subjects who initiated QW darbepoetin alfa (N=129) were white (95%) and/or male (54%), and were mean (SD) 60 (15) years of age. Of the subjects receiving QW darbepoetin alfa, 93% achieved the primary endpoint.

Subjects with ≥1 Hb measurement above 13 g/dL	N = 129	
	n (%)	95% CI
Within 4 weeks	1 (1%)	0%, 4%
Within 6 weeks	2 (2%)	0%, 5%
Within 8 weeks	10 (8%)	4%, 14%

De novo QW darbepoetin alfa dosing achieved the Hb primary endpoint in the majority of subjects, and in this ad hoc analysis, we demonstrate that the Hb target range was achieved by subjects with few excursions above 13 g/dL during the first 8 weeks of therapy.

DE NOVO EVERY-OTHER-WEEK (Q2W) DARBEPOETIN ALFA ADMINISTRATION IN PATIENTS WITH CHRONIC KIDNEY DISEASE (CKD): HEMOGLOBIN (HB) LEVELS ON INITIATION OF THERAPY

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Darbepoetin alfa is an erythropoiesis-stimulating protein (ESP) that can be administered at extended dosing intervals to achieve and maintain Hb levels in study patients with CKD not receiving dialysis.

A combined analysis of two de novo Q2W darbepoetin alfa dosing studies was conducted. In the 24-week study 1 (Suranyi et al, Am J Nephrol. 2003), 85% of all subjects achieved the primary endpoint of Hb within 11-13 g/dL. In the 18-week study 2 (Silver et al. ASN 2005), 92% of subjects achieved the primary endpoint of Hb ≥11 g/dL. The integrated post-hoc analysis presented here was conducted to assess the occurrence of Hb excursions above 13 g/dL during initiation of Q2W darbepoetin alfa therapy.

Patients were enrolled if they were ≥18 years, had Hb levels <11 g/dL, and were iron replete (Studies 1&2), and had CrCl <40 mL/min but were not receiving dialysis (Study 1) or eGFR ≥15 and ≤60 mL/min/1.73 m^2 (Study 2). Subjects initiated Q2W darbepoetin alfa at 0.75 mcg/kg, with subsequent doses titrated to achieve a Hb level between 11 and 13 g/dL.

Enrolled subjects (N=203) were white (56%) and/or female (60%), and were mean (SD) 65 (15) years of age.

Subjects with ≥1 Hb measurement above 13 g/dL	N = 203	
	n (%)	95% CI
Within 4 weeks	1 (0%)	0%, 3%
Within 6 weeks	2 (1%)	0%, 4%
Within 8 weeks	11 (5%)	3%, 9%

Q2W darbepoetin alfa achieved the Hb primary endpoints in the majority of subjects, and in this post-hoc analysis, we demonstrate that de novo Q2W darbepoetin alfa dosing can achieve Hb target ranges with minimal excursions above 13 g/dL during the initiation phase of therapy.

ANALYSIS OF THE RENAL SAFETY OF LONG-TERM ATORVASTATIN USE IN A BROAD SPECTRUM OF PATIENTS

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In the current analysis, safety data from long-term placebo-controlled clinical trials (≥ 1-year in length) of atorvastatin were evaluated to compare rates of renal adverse events (AEs) in atorvastatin-treated patients to those in patients treated with placebo. These data are especially important in the current climate of increased scrutiny on all safety aspects of chronic statin therapy.

Patients from 4 long-term placebo-controlled clinical trials were pooled for this analysis and included a broad spectrum of patients (e.g., post-menopausal women, diabetics, etc.) with varying risks for cardiovascular events. Data were analyzed from 9,394 patients treated with atorvastatin 10–80 mg (4,875) and placebo (4,519). This analysis looked at the occurrence rates of hematuria and albuminuria as there has been heightened awareness of these renal adverse events across the entire statin class within the last couple of years.

Across these 4 placebo-controlled studies, renal AEs were rare and there was no difference between the rates in the atorvastatin and placebo groups. Albuminuria occurred in 62 atorvastatin patients (1.3%) and 82 patients receiving placebo (1.8%). Hematuria occurred in 83 atorvastatin patients (1.7%) and 81 patients receiving placebo (1.8%).

These results demonstrate that renal AEs occurred infrequently with atorvastatin and at a similar rate to placebo. These data provide long-term evidence to support the favorable clinical safety profile of chronic treatment with atorvastatin 10–80 mg in a broad range of patients with varying cardiovascular risk.

EFFECTS OF LANTHANUM CARBONATE ON THE ORAL ABSORPTION AND BIOAVAILABILITY OF CIPROFLOXACIN

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The oral absorption and bioavailability of ciprofloxacin are affected by calcium-containing phosphate binders and sevelamer. This study examined whether a significant pharmacokinetic (PK) interaction exists between lanthanum carbonate (LAN) and ciprofloxacin (CIP).

This was a randomized, open-label, two-way, crossover study. Twelve subjects (6 males, 6 females) were randomly assigned to receive: (A) A single oral dose of CIP 750 mg, and (B) CIP 750 mg (single dose) plus LAN 1 g three times daily with meals for 2 days. Serial blood samples were collected for 24 hours after CIP administration. CIP concentrations were determined using high-performance liquid chromatography. PK parameters of CIP ($AUC_{0-\infty}$, Cmax, Tmax and $t_{1/2}$) with and without LAN were compared to determine the extent and significance of the interaction between the drugs.

PK parameters	CIP	CIP+LAN	(CIP+LAN)/CIP
$AUC_{0-\infty}$ (µg.h/ml)	18 (15-21)*	8.2 (7.1-9.5)*	46% (38-57)
Cmax (µg/ml)	3.3 (2.6-4.2)*	1.4 (1.1-1.8)*	44% (31-62)
$t_{1/2}$ (h)	4.9 (4.6-5.3)	5.4 (5-5.7)	109% (100-119)
Tmax (h)	1.5 (0.75-2)	1.2 (0.5-4.1)	-

*$p<0.01$, CIP vs. CIP+LAN; above data are presented as geometric means and 90% confidence interval (CI) except for Tmax which is presented as median and range. The median difference and 90%CI for Tmax are -0.13 (-0.77-0.51).

The results show that oral absorption and bioavailability of ciprofloxacin are significantly reduced when administered with lanthanum carbonate. Concomitant administration of both drugs should be avoided to prevent possible suboptimal response to ciprofloxacin.

SCREENING FOR CHRONIC KIDNEY DISEASE IN HUMAN IMMUNODEFICIENCY VIRUS: THE RENAL CLINIC PERSPECTIVE

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In June of 2005, the Infectious Disease Society of America released guidelines recommending that all patients with Human Immunodeficiency Virus (HIV) be screened for chronic kidney disease (CKD) with serum creatinine and urinalysis for protein. In 10/05 we began a screening program for CKD in an Infectious Disease Clinic that cares for approximately 1400 patients with HIV. As an adjunct to the program we founded a "CKD in HIV" clinic to handle the associated consults.

Data was obtained through review of clinic and hospital records. We documented patient demographics, health data, HIV & renal specific data, management plans, and outcomes.

There were approximately 36 patients referred to the CKD in HIV clinic during October 2005-September 2006. The rate of referral from the HIV clinic in the first year of screening was approximately 1.4%. The mean age of patients referred was 44 $\pm$ 10. Ninety-three percent of patients were African American and 79% of the patients were male. Nine of 36 (25%) were referred for nephrotic range proteinuria, and 12 of 36 (33%) were referred for non-nephrotic range proteinuria. Ten of 36(28%) were referred for reduced GFR without proteinuria. Two of 36 (5.5%) had advanced CKD. Seven of 36 (19%) never fulfilled their clinic appointment. Nine of 29 patients seen underwent renal biopsy: 3 had HIV associated nephropathy, 3 had Focal segmental glomerulosclerosis, 2 had immune complex disease, and 1had diabetic nephropathy. HIV control was generally good, considering that 65% had undetectable viral loads and 69% had CD4 > 200. Management changes were frequent, including initiation of renin-angiotensin system blockade, modification or initiation of ART and steroid initiation.

A number of referrals have been made to the CKD in HIV clinic. The type of pathology and outcome varied greatly. We feel that a dedicated CKD/HIV clinic has a role in the management of HIV patients.

THE ENDOTHELIAL PATTERN OF INJURY IN GLOMERULOPATHIES (GP) AS ASSESSED BY THE IMMUNOHISTOCHEMICAL (IHC) EXPRESSION OF VON WILLEBRAND FACTOR(vWF), CD 31 AND CD 34

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An endothelial pattern of injury is the hallmark of malignant hypertension, hemolytic uremic syndrome or vasculitis. The aim was to assess glomerular and interstitial endothelial involvement by studying vWF, CD31 and CD34 in GP.

A cross-sectional study of 36 patients(pts) with GP was performed. Mean age was 46.44±12.97, 22M. HE, PAS and Trichrome GÖmÖri, as well as IHC (vWF, CD31, CD34) were done on kidney biopsy. IHC was graded on a scale ranging from 0 to 3. BP, proteinuria and serum Cr were measured. Statistical analysis was done using SPSS 10.

Histology: 3 pts: crescentic (2 primary, 1 vasculitis), 11 pts: FSGS(all primary), 5 pts: MN(1 SLE), 1pt: membranoproliferative GP(lymphoma), 11 pts: mesangial proliferative GP(all primary), 5 pts: MCD(all primary). Overall, correlations were:

Parameter	Parameter	Correlation Coefficient(Spearman's)	p-value
CD34 glomerular endothelium(GE)	CD31 GE	r=0.60	p=0.001
CD34 GE	vWF GE	r=-0.18	p=0.19
CD34 interstitial vessels(IV)	CD31 IV	r=0.26	p=0.13
CD34 IV	vWF IV	r=0.13	p=0.28
CD34 IV	Proteinuria(P)	r=-0.006	p=0.48
CD31 IV	P	r=-0.09	p=0.34
vWF IV	P	r=0.57	p=0.003

Our results show microvasculature involvement in GP.The markers CD34, CD31 and vWF are differentially affected. Underlying this could be: downregulation/loss versus upregulation, release from cryptic sites and aberrant expression due to matrix alterations. This might explain why loss of the markers was most evident in fibrosclerotic lesions.

DO PROPHYLACTIC ANTIBIOTICS ENSURE PROTECTION IN THE SURGICAL CURE OF DENTAL FOCI IN PATIENTS WITH CHRONIC GLOMERULAR DISEASE AS ASSESSED BY THE DYNAMICS OF URINARY N-ACETYL-β-D-GLUCOSAMINIDASE (NAG)?

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Infectious dental foci (IDF) are often overlooked in the pathogenesis of chronic glomerulopathies (CG). Urinary NAG, a marker of tubular injury, is increased in CG and may identify patients (pts) at greater risk of GFR decline. The aim of the study was to assess the role of prophylactic antibiotics in the surgical cure of IDF in pts with CG.

Eighteen pts, 9M, 9F, mean age: 40.1±13.1 with CG and IDF were enrolled into the study. All pts underwent periodontal surgery under antibiotic coverage; 8 healthy subjects served as controls. We evaluated urinary NAG, proteinuria, serum Creatinine (SCr) and GFR (MDRD) at baseline and at 1, 3 and 7days thereafter. NAG was assessed colorimetrically and expressed as U/gCr. NAG in controls: 1.72±0.85U/gCr. Statistical analysis was done using EpiInfo6 and SPSS 10.

Results:

Parameter	Baseline	at 1 day	at 3 days	at 7 days	p value ANOVA
NAG(U/gCr)	12.06± 9.85*	12.12± 7.1	12.35± 6.97	11.52± 7.02**	p>0.05
Proteinuria (gms/24h)	3.53±2.27	3.67± 2.18	3.68±2	3.44± 1.88	p>0.05
SCr (mg%)	2.39±2.48	2.6± 2.24	2.55± 2.8	2.58± 2.9	p>0.05
GFR(ml/min/1.73 m^2BS)	57.33± 37.23	53.88± 35.63	56.41± 35.02	59.56± 37.99	p>0.05

p^*=0.0073 (as compared to controls); p^{**}=0.0007(as compared to controls)-unpaired t-test

Prophylactic antibiotics did not prevent interactions of IDF with the kidney.

DENOVO MONTHLY DOSING WITH DARBEPOETIN ALFA

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Previous reports have described initial dosing of ESA's at 1-2 week intervals with eventual migration to monthly dosing interval. However, initial dosing interval of four or more weeks has only rarely been described. Herein we describe a simplified regimen featuring denovo monthly dosing with darbepoetin alfa.

One of us (RPG) treated anemia patients with CKD States 3 and 4 routinely with denovo monthly dosing. Twenty charts were available for retrospective review.

Demographic Data: Mean age 75.6; 11 female, 9 male

Treatment Data (mean values): Initial Hgb 10.9
Final Hgb (4mos) 11.8
Initial Dose 106 mcg
Final Dose 117 mcg

The median initial and final dose was 100mcg.

There were no treatment related adverse events.

In conclusion anemic CKD patients can be treated effectively with monthly darbepoetin dosing from the beginning of treatment. Most patients can be treated with a standard dose of 100mcg monthly. This simplified regimen is amenable to treatment of both office administered and home treated patients.

Further study of larger numbers of patients is suggested by this initial experience.

BARRIERS TO FOOD ACQUISITION IN HEMODIALYSIS PATIENTS Teresa Gerbeling, Jackie Carder, Tammy Burton-Fikar, Jen Strong. Dialysis Center of Lincoln, Inc. Lincoln, Nebraska, USA.

The inability of hemodialysis (HD) patients (pts) to obtain and prepare food is associated with compromised nutritional status. The purpose of this project was to describe the percent of pts with an albumin < 4.0 g/dL (bromocresol green) that 1. run out of money to purchase food; 2. need assistance preparing food; 3. need assistance shopping for food; and 4. follow the recommendation of the RD after 3 months. Questionnaires were administered by an RD to all in-center HD pts at a midwestern dialysis center that met the following criteria: living independently, dialysis vintage > 3 months and at least 18 yoa. With a 4 point Likert scale ranging from always to never, pts were asked 3 questions. All responses except "never" were considered affirmative and a nutritional intervention was implemented. Of the 57 pts meeting the criteria, 14 (25%) answered affirmative to at least one question. The following description applies to these 14 pts: 50% were male; mean age 64±11(SD) yrs; avg dialysis vintage 59±51 (SD) mons.

Question	Intervention Options	% pts answering affirmative
Do you run out of money to buy food?	1. food pantry 2. meals on wheels referral; 3. rx for supplement	12
Do you need help shopping for food?	1. rx for supplement; 2. meals on wheels; 3. grocery delivery	14
Do you need help preparing food?	1. rx for supplement 2. meals on wheels referral	11

The RD made the following # of recommendations: food pantry: 7; meals on wheels referral: 14; nutritional supplement: 14; grocery delivery: 1. None of the pts followed the recommendation for food pantry or grocery delivery. One pt (7%) signed up for meals on wheels and 5 pts (36%) followed the recommendation for a supplement. RDs working with in-center HD pts need to routinely assess pts for barriers to obtaining and preparing food. Pt education regarding increasing calories and protein in food consumed, may be better accepted than the interventions used in this study. An assessment of pt beliefs and attitudes regarding alternative interventions may be beneficial.

EFFICACY OF C.E.R.A., A CONTINUOUS ERYTHROPOIETIN RECEPTOR ACTIVATOR, IN TREATMENT OF RENAL ANEMIA: OVERVIEW OF 6 GLOBAL PHASE 3 TRIALS

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C.E.R.A. is a continuous erythropoietin receptor activator with unique receptor activity and a prolonged half-life allowing extended dosing intervals. Six global Phase III studies in >2400 patients compared C.E.R.A. with epoetin alfa or beta (EPO-α or –β) or darbepoetin-α (DAR). All were randomized, open-label, multicenter, parallel-group trials. Two initiation studies enrolled therapy-naïve patients. In AMICUS (N=181), dialysis patients initially received CERA Q2W or EPO-α or -β TIW IV for 24 wks initiation followed by a 28-wk extension in which CERA was dosed Q2W or Q4W. In ARCTOS (n= 324), nondialysis patients received C.E.R.A. Q2W or DAR QW for 18 wks correction and 10 wks evaluation, followed by C.E.R.A. Q2W or Q4W for a 24-wk extension. In both studies, C.E.R.A Q2W successfully corrected anemia and maintained Hb levels in naïve patients. Four maintenance studies evaluated switching of dialysis patients from EPO or DAR to C.E.R.A. In MAXIMA (IV, N=673) and PROTOS (SC, N=572), dialysis patients received C.E.R.A. Q2W or Q4W or continued on EPO-α or –β TIW for 28 wks titration, 8 wks evaluation, and an additional 16-wk safety period. In STRIATA (IV, N=313), dialysis patients received C.E.R.A. Q2W or DAR QW or Q2W for 28 wks titration, 8 wks evaluation, and an additional 16-wk safety period. In RUBRA (IV or SC, N=336), dialysis patients received C.E.R.A. in pre-filled syringes Q2W or Q4W or continued on EPO. C.E.R.A. successfully maintained stable Hb levels whether administered SC or IV. C.E.R.A.'s efficacy mirrors that of EPO or DAR but requires less frequent administration.

C.E.R.A. ONCE MONTHLY MAINTAINS STABLE HB LEVELS IN PATIENTS WITH CKD ON DIALYSIS WITH AND WITHOUT CONGESTIVE HEART FAILURE (CHF)

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C.E.R.A., a continuous erythropoietin receptor activator with unique receptor activity and a long half-life, is currently in development to provide correction of anemia and stable Hb levels at intervals up to once monthly.

A post-hoc analysis of two Phase III studies assessed the efficacy of C.E.R.A. administered IV or SC up to Q4W for maintaining target Hb in patients on dialysis with or without CHF directly converted from IV or SC epoetin alfa or beta TIW-QW. As with other phase III clinical trials in this therapeutic area, class IV CHF patients were excluded from this study protocol. A total of 413 patients received C.E.R.A. Q2W, 415 received C.E.R.A. Q4W and 417 continued with epoetin TIW-QW. Dose was adjusted to maintain baseline Hb ±1.0 g/dL of baseline and 10.0-13.5 g/dL. Mean Hb change between baseline and the evaluation period (weeks 29-36) for patients treated with C.E.R.A. Q4W or epoetin TIW-QW with and without CHF is reported.

A total of 20% of patients treated with C.E.R.A. Q4W or epoetin had CHF at baseline. Mean baseline Hb levels were similar for C.E.R.A. and epoetin. During the evaluation period, mean Hb levels were similar in patients with and without CHF (C.E.R.A. Q4W: 11.6 vs 11.7 g/dL; epoetin: 11.7 vs 11.7g/dL). C.E.R.A. Q4W effectively maintained Hb levels from baseline to evaluation in patients with and without CHF: mean changes were –0.14 and –0.03 g/dL, respectively. Mean Hb change was –0.13 and –0.06 g/dL for epoetin-treated patients with and without CHF, respectively. Patients in both study arms with and without CHF had similar AE profiles.

These Phase III data indicate that C.E.R.A. is effective for maintaining stable Hb levels in patients on dialysis with and without CHF who convert directly from epoetin TIW-QW.

LACK OF ASSOCIATION OF CONVENTIONAL CARDIOVASCULAR SCREENING TESTS WITH SURVIVAL OF PATIENTS ON HEMODIALYSIS (HD)

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Cardiovascular (CV) disease is the leading cause of death among patients on dialysis. The rates of screening for CV disease are low in patients on dialysis. This may be due to lack of belief in utility of screening measures to control CV deaths in this population. Of 64,962 patients starting HD between 1/1/96-10/31/2000 and surviving the first year, only 12,890 (19.8%) were screened by a stress test or coronary angiogram for CV disease within the first year after initiation of HD. We evaluated the characteristics of patients that did and did not undergo screening and association of CV screening with patient survival.

Of the 60, 841 patients not listed for a kidney transplant and without a prior history of ischemic heart disease, 11,453 (18.8%) underwent any screening. Only 20% of the patients with history of cardiac disease such as cardiac arrest, cardiac arrhythmia or heart failure, or risk factor for heart disease such as hypertension, diabetes or stroke were screened. Twelve percent of patients with functional incapacity were screened. There was no association of screening with patient survival by Kaplan-Meier analyses and only a small effect in a multivariate model adjusted for known risk factors for death (HR: 1-1.1, $p<0.001$).

Our analyses demonstrate lack of association of traditional risk factors with likelihood of cardiac testing and also lack of demonstrable benefit of screening on patient survival. But in the absence of a randomized controlled trial it is difficult to preclude the possibility of indication bias, and therefore we cannot exclude a benefit in screening related to unmeasured factors.

EFFICACY OF CHOLECALCIFEROL (VITAMIN D_3) THERAPY IN CORRECTING VITAMIN D INSUFFICIENCY AND SECONDARY HYPERPARATHYROIDISM IN PATIENTS WITH CHRONIC KIDNEY DISEASE: A RANDOMISED, PLACEBO CONTROLLED STUDY

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Correction of vitamin D insufficiency by vitamin D supplementation in chronic kidney disease (CKD) stages 3 & 4 patients has been recommended by the National Kidney Foundation; however, limited data are available to determine its effectiveness in treating secondary hyperparathyroidism. This randomized, controlled, double-blinded pilot study investigated the efficacy of cholecalciferol to raise serum 25-hydroxyvitamin D (25(OH) D) levels and reduce parathyroid hormone (PTH) levels in subjects with CKD. Subjects with CKD stage 3 and 4 (GFR 15-59 ml/min/1.73 m^2), vitamin D insufficiency (serum 25(OH)D <30 ng/mL) and serum PTH > 70 pg/mL were randomized to either 50,000 IU of cholecalciferol or placebo once a week for 12 weeks. 20 subjects finished the study, 10 subjects in both the placebo and cholecalciferol groups. Baseline racial distribution, age, GFR, PTH, and 25(OH)D concentrations were comparable in both study groups. After 12 weeks of therapy, all except one cholecalciferol-treated subject in the active treatment group became vitamin D sufficient. The mean serum 25(OH)D concentrations increased significantly from 17.3 [95% CI: (11.8,25.2)] to 49.4 [95% CI: (33.9,72.0)] ng/mL (+213%, $p<0.0001$) in cholecalciferol-treated subjects (baseline to week 12). In contrast, no significant change occurred in serum 25(OH)D values in placebo treated subjects over time. PTH levels in cholecalciferol treated subjects decreased by 31% from baseline values as compared to only 7% decrease in placebo treated subjects ($p=0.14$). Weekly supplementation of cholecalciferol is an effective method to correct vitamin D status in CKD stage 3 and 4 patients, and may be effective in reducing PTH levels.

LONG-TERM FOLLOWUP OF PATIENTS WITH ANEMIA OF CKD TREATED WITH ONCE MONTHLY (QM) DE NOVO DARBEPOETIN ALFA (DA). Elias Chalhoub, Khaled Ismail, Mark D. Faber, Rami Fayad, Stanley Frinak, Jerry Yee. Henry Ford Hospital, Detroit, MI, USA.

Successful Q4 wk DA therapy has been proven to treat anemia of CKD for up to 6 mo duration, (Ling et al, Clin Nephrol 63:327–34, 2005). However, QM DA therapy for longer durations is unproven. This report represents 10 mo of followup of 68 erythropoietin stimulating agent (ESA)-naïve CKD stage 3–5 patients whose anemia was managed by CAMP© (Computer Anemia Management Program), an algorithm that coordinately prescribes QM DA with iron to optimally attain and maintain a target Hb of 11–13 g/dL.

Organ transplant recipients and subjects on immunosuppressant agents were excluded. Transferrin saturation (TSAT), ferritin, DA dose, and Hb were obtained QM. Age, bodyweight, presence/absence of proteinuria and diabetes were recorded. Statistical analysis by ANOVA was carried out on parameters at study initiation and termination, with 2-tailed t-test for between group comparisons. Responders (R) were designated as those who achieved a Hb ≥11 g/dL and non-responders (NR) as those who did not.

A mean of 9.2±2.6 DA doses was delivered over 301±74 d, with final Hb attained as follows: <11 g/dL (38.3%), 11–13 g/dl (60.3%) and >13 g/dl (1.5%). Differences between R and NR were found for TSAT (34.4±11.7% *v* 25.1±9.3, P≤0.01), DA dose (82±72mcg *v* 193±100, P≤0.01) and number of DA doses (10.0±2.3 *v* 8.6±2.9, P<0.03). We conclude that QM DA achieved the Hb target in 60.3% of subjects after 300 d of therapy. This trial reflects the efficacy of using automated methods for the management of the anemia of CKD using QM DA. We also content that longer duration of therapy, more aggressive iron therapy and higher QM DA doses may enhance NR's outcomes.

Variable	Initial	Mid 135±65 d	Final 301±74 d	P value
Hb (g/dL)	10.0±0.8	11.0±1.3	11.1±1.1	<0.0001
TSAT (%)	26.5±13.4	29.2±11.7	30.9±11.7	<0.003
Ferritin (ng/mL)	278±287	270±247	267±226	>0.5
DA dose (mcg)	96±43	116±93	124±99	<0.01

SAFETY AND EFFICACY OF FERUMOXYTOL AS AN INTRAVENOUS IRON REPLACEMENT THERAPY: RESULTS FROM A PHASE III STUDY OF CHRONIC KIDNEY DISEASE (CKD) PATIENTS NOT ON DIALYSIS

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Iron deficiency anemia is common in non-dialysis dependent CKD (NDD-CKD) patients. Oral iron is poorly tolerated and ineffective. Current IV irons are impractical and have limited efficacy and significant side effects. Ferumoxytol is a new semisynthetic, carbohydrate-coated iron oxide nanoparticle. Due to a low level of free iron and isotonicity, ferumoxytol can be administered as a rapid IV injection at doses of up to 510 mg in 17 seconds.

In a safety and efficacy study (ClinicalTrials.gov NCT00255424), 304 NDD-CKD patients were randomized 3:1 to 2 x 510 mg doses of ferumoxytol IV or 200 mg of elemental oral iron daily for 21 days. The change in hemoglobin (Hb) from baseline at day 35 was significantly higher in the ferumoxytol group in both the Intent to Treat (ITT) (ferumoxytol 0.81g/dl vs. oral iron 0.21g/dl, $p = 0.0002$) and Efficacy Evaluable (EE) (ferumoxytol 0.86g/dl vs. oral iron 0.06 g/dl, $p<0.0001$) populations. All primary and secondary endpoint analyses were statistically significant in both ITT and EE populations, and remained significant when patients were stratified by usage of Erythropoiesis Stimulating Proteins (ESPs). For patients treated with a stable dose of ESP and ferumoxytol vs. ESP and oral iron, the mean Hb change was +1.20 vs. -0.12 g/dl ($p = 0.0015$), respectively. In patients treated with ESP and ferumoxytol 61.0% achieved at least a 1g/dl rise in Hb vs. 16.7% for oral iron ($p = 0.001$). For the non-ESP group, the mean Hb change was 0.70 g/dl for ferumoxytol vs. 0.15 g/dl for oral iron ($p = 0.0038$). Related adverse event rate was 10.6% in the ferumoxytol group vs. 24.0% in the oral iron group. No drug-related SAEs were observed.

In this study, ferumoxytol offered rapid and efficient IV iron replacement in the NDD-CKD patient population.

A DOUBLE-BLIND, PLACEBO-CONTROLLED, RANDOMIZED PHASE III STUDY OF THE SAFETY OF FERUMOXYTOL AS A NEW INTRAVENOUS IRON REPLACEMENT THERAPY

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Iron deficiency anemia is common in patients with CKD. Ferumoxytol is a semisynthetic carbohydrate coated iron oxide nanoparticle being developed as a new intravenous iron therapy to treat anemia in CKD patients. Ferumoxytol is designed to provide bioavailable iron with low levels of free iron and low immunological reactivity in an isotonic formulation, and can consequently be given in doses of 510 mg as an injection at a rate of 30 mg/second (a 17 second injection). A recently presented Phase III study of ferumoxytol in non-dialysis dependent CKD patients showed ferumoxytol to have a safety profile comparable to oral iron without any drug-related Serious Adverse Events (SAEs).

An additional multicenter Phase III study (ClinicalTrials.gov identifier NCT00255450) to evaluate the safety of a single dose of IV ferumoxytol compared with placebo using a double-blind, crossover design in 750 patients with non-dialysis dependent or dialysis-dependent CKD has been completed. Patients were randomly assigned to receive either ferumoxytol (in a single blinded dose of 510 mg in 17 ml @ 1 ml per second) or placebo (sterile 0.9% saline in a single blinded dose of 17 ml @ 1 ml per second) on day zero, and then crossed over to the other (blinded) therapy on day seven. The observation period ended on day fourteen.

CKD patients, $\geq$18 years old, were included if Hemoglobin $\geq$ 9.0 and $\leq$ 12.5 g/dL, transferrin saturation $\leq$ 50% and serum ferritin $\leq$ 600 ng/ml. Patients had received no parenteral or oral iron therapy within 5 days. Safety evaluation included medical history, physical exams, vital signs, laboratory results and adverse events (AEs). All AEs were captured between day zero and study completion on day fourteen.

AN EXAMINATION OF DIRECT AND INDIRECT EMPLOYER COSTS ASSOCIATED WITH EPOETIN ALFA TREATMENT IN PRE-DIALYSIS CHRONIC KIDNEY DISEASE PATIENTS

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Anemia is a common hematologic disorder often associated with a variety of chronic diseases. Within an insured population, CKD is generally believed to be the chronic disease most often associated with anemia. This study assessed the employer cost burden of anemia of CKD for a major U.S. manufacturer by examining the costs and effects of anemia of CKD and its treatment with epoetin alfa (EPO). Hemoglobin (Hb) levels, direct costs, and indirect costs for patients with anemia of CKD were collected for 15 months (9 months pre-EPO treatment and 6 months concurrent or post-EPO treatment). Pre-treatment and post-treatment periods were compared. Direct costs (healthcare costs) included medical and pharmacy costs, while indirect costs included absenteeism (work days lost) and presenteeism (a decrease in work productivity due to illness). Presenteeism was measured by SKU (stock keeping units), a unique numeric identifier commonly used in tracking parts and specific product inventory. These numbers are used as a proxy for individual worker productivity in settings where employees install the relevant SKU. Treating anemia of CKD with EPO reduced healthcare costs by $4,417 per patient per year (PPPY), decreased absenteeism by 52.3 days PPPY, and increased productivity by 91.5% PPPY. Treatment with EPO increased mean Hb levels from 9.4 g/dl to 12.2 g/dl during the 6-month EPO treatment period. Hemoglobin level was significantly correlated with both healthcare and productivity costs: as Hb increased, healthcare costs decreased, and productivity increased. In this study, EPO treatment was associated with increased Hb levels, decreased direct employer costs and improved productivity.

STATINS DECREASE THE RISK OF MYOCARDIAL INFARCTION, CORONARY HEART DISEASE AND VASCULAR EVENTS IN PATIENTS WITH RENAL FAILURE. A META-ANALYSIS

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Objective: Although the role of statins in improving cardiovascular outcomes is well established, their role in patients with renal insufficiency is uncertain. We performed a meta-analysis of randomized clinical trials to evaluate the role of statins in renal failure patients (CKD stage 2 and above) in primary prevention of vascular events, myocardial infarction and coronary heart disease.

Methods: Randomized controlled trials that analyzed cardiovascular outcomes in patients with renal failure were included for the meta-analysis. A total of 21,770 patients from five trials were analyzed. Chi-square test was used to assess inter-study heterogeneity. Relative risk across all studies was determined by meta-analysis with Mantel-Haenszel random-effects model.

Results: Statins were associated with significant relative risk reduction in myocardial infarction, coronary heart disease ($p<0.001$) and vascular events ($p<0.02$) in patients with renal failure. The relative risk for MI and CHD was 0.77 (9.69-0.855: 95% CI) and total vascular events was 0.82 (0.70-0.96: 95% CI) in our meta-analysis.

Conclusion: Statins significantly reduce the risk for coronary heart disease, myocardial infarction and total vascular events in patients with renal failure. Though protienuria was not analyzed in our meta-analysis, this reduction in CHD and MI might be explained by the pleiotropic effects of statins which include reduction in systemic inflammation, improvement in renal blood flow and endothelial function and inhibition of protein uptake in the proximal tubules.

CARDIAC TROPONIN I HAS LOW NEGATIVE PREDICTIVE VALUE FOR THE DETECTION OF OCCLUSIVE CORONARY ARTERY DISEASE IN PATIENTS WITH RENAL FAILURE

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Background: Cardiac troponin I (cTnI) is considered the most sensitive and specific diagnostic marker in patients with renal failure. The diagnostic utility of cTnI can differ in patients with renal failure with and without hemodialysis.We assessed the positive and negative predictive values of cTnI in patients with acute coronary syndrome.

Methods: Retrospective study (n=108) of patients with renal failure who underwent a diagnostic coronary angiogram were included for the study. Patients were divided into Group I (renal insufficiency without the need for hemodialysis=76) and Group 2 (renal insufficiency patients on hemodialysis=32). Cardiac troponin I was quantified using Access Accu TnI method. Positive angiogram was defined as newly diagnosed greater than 70% luminal occlusion in any one coronary artery. Positive and negative predictive values were calculated using the Bayesian Analytical model.

Results: Cardiac troponin I has 90% positive predictive value (PPV) and 29% negative predictive value (NPV) in patients not on hemodialysis. The positive likelihood ratio (PLR) was 2.18 (1.25-3.78: 95% CI) and negative likelihood ratio (NLR) was 0.59 (0.40-0.76: 95%CI) in group 1. In group 2 cTnI has a PPV of 95% and NPV of 49% with PLR of 5.675 (2.45-13.1: 95% CI) and NLR of 0.43 (0.34-0.53: 95% CI).

Conclusion: Elevated cTnI signifies occlusive coronary artery disease in patients with renal failure. Alternatively, normal levels of cTnI cannot rule out obstructive coronary artery disease in patients with renal failure. The NPV of cTnI is lower in patients with renal failure not requiring hemodialysis when compared to patients on hemodialysis.

EFFECT OF BASELINE ESTIMATED GLOMERULAR FILTRATION RATE (eGFR) ON THE EFFICACY OF ONCE-MONTHLY (QM) DARBEPOETIN ALFA IN THE MAINTENANCE OF HEMOGLOBIN (HB) LEVELS IN PATIENTS WITH CHRONIC KIDNEY DISEASE (CKD)

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Darbepoetin alfa is an erythropoietic protein previously shown to maintain Hb levels at a QM dosing interval in CKD patients not receiving dialysis who were previously stable on every-other-week (Q2W) darbepoetin alfa (Ling et al, *Clin Nephrol.* 2005 [Study 1]; Agarwal et al, *J Intern Med.* 2006 [Study 2]). The current, combined analysis was conducted to determine the impact of baseline eGFR on the efficacy of QM darbepoetin alfa in CKD patients.

The two studies were 29 weeks (Study 1) or 33 weeks (Study 2) in duration. Efficacy was assessed from weeks 21-29 (Study 1) or 25-33 (Study 2). Enrolled subjects had Hb levels 10-12 g/dL (Study 1) or 11-13 g/dL (Study 2), CrCl (mL/min) >15 and <40 (Study 1) or eGFR (mL/min/1.73 m^2) ≥15 and ≤60 (Study 2), and adequate iron levels, and were receiving stable, Q2W darbepoetin alfa (≤25% change in dose in the previous 6 weeks). QM darbepoetin alfa was initiated at twice the Q2W dose; subsequent doses titrated to maintain Hb levels within the 10-12 or 11-13 g/dL ranges. Subjects were considered to have achieved the primary endpoint if mean Hb during evaluation for each study was 10-12 g/dL (Study 1) or ≥11 g/dL (Study 2). Logistic regression analysis assessed the effect of baseline eGFR, Hb, and/or diagnosis of diabetes mellitus (DM) on achieving the primary endpoint for each study (yes/no based on the respective study definitions; eGFR calculated for all subjects).

Subjects included in this combined analysis (N=247) were mean ±SD 67±13 years; the majority were white (56%) and/or female (54%). Overall, there was no significant effect of baseline eGFR on achievement of the primary endpoints ($P > 0.3$): $P = 0.63$ including eGFR, Hb, and DM status (significance level 0.10); $P = 0.62$ including eGFR and Hb; and $P = 0.34$ including only baseline eGFR.

These results demonstrate that there was no effect of baseline eGFR on the efficacy of QM darbepoetin alfa in the maintenance of Hb levels in study subjects with CKD not receiving dialysis. In addition, the efficacy of QM darbepoetin alfa was maintained when baseline Hb level and diagnosis of DM were included in the model.

EFFECTS OF CINACALCET ON EMESIS AND CEREBRAL BLOOD VOLUME

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Purpose: Calcimimetics were developed for treating hyperparathyroidism. Some patients taking calcimimetics experience emesis, but the reasons for this are not well understood.

Methods: Real-time RT-PCR, receptor binding assays, and animal studies such as the ferret emesis model and phMRI imaging of the rat brain were used.

Results: Real-time RT-PCR studies showed that calcium sensing receptor (CaR) was expressed at a very low level in human brain and heart, while no detectable CaR was observed in primary cultures of human coronary artery and aortic endothelial and smooth muscle cells, nor in neonatal mouse cardiomyocytes.

When cinacalcet, one of the newly developed calcimimetics, was administered orally to ferret, emesis was observed at 30 mg/kg. Furthermore, when awake rats were treated with cinacalcet intravenously at 30 mg/kg and brain activation patterns were assessed using phMRI, cinacalcet reduced cerebral blood volume in several brain regions including area postrema/nuclues tractus solitarius that are known as the emetic center in the brainstem.

In a panel of 77 in vitro protein binding assays, while cinacalcet had no effect on a majority of proteins, binding activities were observed at more than ten transmitter receptors, ion channels and transporters such as dopamine receptor, histamine H_2 receptor, muscarinic receptor, 5-hydroxytryptamine1A (5-HT1A) and haloperidol-sensitive sigma sites.

Conclusions: The potential effects of cinacalcet on emesis and the CNS are possibly mediated by its non-specific interactions with various ion channels and transmitter receptors other than CaR. The long-term side effects of calcimimetics on the CNS require further investigation.

THE EPITHELIAL SODIUM CHANNEL SUBUNIT STOICHIOMETRY

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Ion channels, including the epithelial Na^+ channel (ENaC), are intrinsic membrane proteins comprised of component subunits. Proper subunit assembly and stoichiometry are essential for normal physiological function of the channel protein. ENaC is comprised of three subunits, α, β and γ, that have common tertiary structures and much amino acid sequence identity. For maximal ENaC activity, each subunit is required. The subunit stoichiometry of functional ENaC within the membrane remains uncertain. We combined a biophysical approach, fluorescence intensity ratio (FIR) and fluorescence resonance energy transfer (FRET) analysis, used to assess relative subunit stoichiometry with total internal reflection fluorescence (TIRF) microscopy, which enables isolation of plasma membrane fluorescence signals, to determine the limiting subunit stoichiometry of ENaC within the plasma membrane. Our results demonstrate that membrane ENaC contains equal numbers of each type of subunit and that at steady-state, subunit stoichiometry is fixed. Moreover, we find that when all three ENaC subunits are co-expressed, heteromeric channel formation is favored over homomeric channels.

ENaC, similar to other types of ion channels, is sensitive to membrane phosphatidylinositide levels. In particular, $PI(3,4,5)P_3$ binds to β- and γ- but not α-ENaC to stabilize channel gating and directly increase open probability. Here we titrated mutant and wild-type subunit levels in combination with an electrophysiology readout of channel activity to determine the stiochiometric contribution of β- and γ-ENaC subunits to the integral $PI(3,4,5)P_3$ biding site within the channel. The activity in the absence and presence of PI3-K signaling of ENaC containing two distinct mutations in the β- or γ-subunit binding site were compared to channels containing all wild-type subunits. Electrophysiological results testing effects of ENaC subunit dose on channel activity were consistent with TIRF-FIR and FRET findings and confirmed preferential formation of heteromeric channels containing equal numbers of each subunit.

ACUTE REGULATION OF THE EPITHELIAL SODIUM CHANNEL BY PHOSPHATIDYLINOSITOL 3-KINASE IN ISOLATED COLLECTING DUCT PRINCIPAL CELLS

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ENaC activity is rate limiting for Na^+ reabsorption across the distal nephron. Plasma electrolyte and volume are fine-tuned at this site. Thus, ENaC activity plays an important role in control of blood pressure. ENaC is a target for PI3-K and its down-stream phospholipid-dependent kinase effectors, including Sgk. Sgk increases membrane levels of ENaC to increase channel activity. Emerging evidence suggests that there is close spatiotemporal coupling between PI3-K and ENaC with the kinase also influencing channel gating independent of Sgk. To further study acute regulation of ENaC by PI3-K, we isolated cortical collecting ducts (CCD) from rats maintained on a low sodium diet and used patch-clamp electrophysiology to assess the single channel properties of ENaC in this preparation. Inhibition of PI3-K with either wortmannin or LY294002, but not the inactive analogue LY303511, rapidly (~1 min.) decreased ENaC open probability and activity. These compounds elicited an identical response in the immortalized cortical collecting duct cell line, MPK_{CCD14}. Insulin-like growth factor-I (IGF-I) increased Na^+ reabsorption across MPK_{CCD14} epithelia cells via PI3-K with LY294002 completely abolishing IGF-I actions on transport. In contrast, MAPK and Rho-kinase inhibitors PD98059 and H1152, respectively, had no effect on IGF-I induced Na^+ transport. However, the PTEN inhibitor bpV(pic) lessened inhibition of Na^+ transport by LY294002 stressing the importance of the equilibrium between production of PIP_3 by PI3-K and metabolism of this phospholipid by PTEN to acute regulation of ENaC activity. These results are important for they are the first to demonstrate in a native preparation that PI3-K acutely influences ENaC gating likely through a mechanism independent of Sgk.

SOLUBLE HB-EGF MODULATES E-CADHERIN TRANSCRIPTIONAL REPRESSORS AND STIMULATES EMT IN IMCD CELLS

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EGF receptor activation enhances epithelial-to-mesenchymal transition (EMT) in a synergistic manner with TGF-β. HB-EGF is upregulated following acute ischemic/toxic renal injury, particularly in the distal nephron, and may contribute to EMT during the process of tubular regeneration. This work investigates the effect of HB-EGF on tubular epithelial cells with respect to EMT. Mouse inner medullary collecting duct (IMCD) cells were stably transfected to overexpress soluble HB-EGF ($IMCD^{sHB}$) which led to significant changes in cellular morphology (membrane ruffling, cytoplasmic projections, and lack of tight colony formation). EMT was demonstrated by the loss of epithelial markers E-cadherin and cytokeratin, and the appearance of Fsp-1 by Western blot and immunofluorescence. In addition, $IMCD^{sHB}$ cells gained the property of anchorage-independent growth in soft agar. A luciferase expression assay and RT-PCR was used to determine that E-cadherin is downregulated by sHB-EGF at the transcriptional level in a TGF-β-indepdendent manner. Quantitative real-time PCR was used to evaluate known E-cadherin transcriptional repressors, of which Snail-2 (Slug) was the most dramatically upregulated, with transcript levels in $IMCD^{sHB}$ cells exceeding IMCD cells by > 25-fold. Because growth factor overexpression in vitro may mimic chronic rather than acute injury in vivo, we analyzed mouse kidney tissue after 7 days of unilateral ureteral obstruction. Quantitative PCR demonstrated upregulation of both HB-EGF and TGF-alpha in obstructed kidneys. Similar to the in vitro data, while several E-cadherin transcriptional repressors were upregulated in our model of chronic injury, the quantity of Snail-2 transcript was greatest. In conclusion, EGFR activation by ligands such as HB-EGF and TGF-alpha following renal injury may lead to EMT through modulation of E-cadherin transcriptional repressors, most notably Snail-2.

P53 OPPOSES GDNF-MEDIATED GROWTH SIGNALING DURING EARLY KIDNEY DEVELOPMENT. Zubaida Saifudeen, Jana Stefkova, Susana Dipp, Samir S. El-Dahr. Department of Pediatrics, Tulane Health Sciences Center, New Orleans, LA.

Metanephric kidney development ensues by reciprocal interactions between the ureteric bud (UB) and the metanephric mesenchyme (MM). The MM releases the glial-derived neurotrophic factor (GDNF) at E9.5 that activates a receptor tyrosine kinase (c-Ret) expressed by the nephric duct, resulting in outgrowth of the UB at E10.5. We report here that p53-null mice exhibit multiple defects in early renal development, including duplex ureters/kidneys. *p53* is abundantly expressed in the nephric duct at E10.5. By E13.5, *p53* is expressed in the UB tree including stalks and tips as well as in nephron progenitors, whereas the mesenchyme expresses little *p53*. To determine whether the renal phenotype in conventional p53-null mice is due to loss of p53 function in epithelia- vs. metanephric mesenchyme, we conditionally inactivated p53 from each metanephric component by Cre-mediated recombination or over-expression of dominant negative p53. The duplex ureter/kidney and abnormal patterning phenotype was recapitulated in mice with conditional inactivation of the *p53* gene in the UB lineage but not in mice with *p53* inactivation in the MM. p53 inactivation from the UB resulted in a larger renal medulla and papilla in newborn mice kidneys, with UB branches that have failed to undergo terminal differentiation as determined by lack of differentiation markers. Pharmacologic inhibition of p53 (Pifithrin, 10μM) in cultured E12.5 kidneys resulted in a significant increase in branching, up to 75% more peripheral tips and increased kidney size compared to the control contra-lateral kidney. RT-PCR and in situ hybridization revealed up-regulation of GDNF, c-Ret and its downstream effector Wnt11. Significantly, sensitivity of nephric ducts to GDNF was enhanced by pharmacologic or genetic p53 inactivation, resulting in ectopic budding in response to sub-threshold doses of GDNF. Conversely, pharmacologic activation of p53 in the duct (Nutlin, 10μM) abrogated budding to high doses of GDNF, which cause robust budding in control ducts. These findings suggest a model of negative regulation where by p53 in the nephric duct and UB restricts the proliferative potential of the GDNF→c-Ret→Wnt11 pathway.

ANTI-PR3 IMMUNE RESPONSE MEDIATES RENAL INJURY

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Wegener's Granulomatosis (WG) is a debilitating and life-threatening disease of unknown etiology, and a major cause of pauci-immune necrotizing and crescentic glomerulonephritis. In WG, there is a strong and specific association with autoantibodies directed against proteinase 3 (PR3). The pathogenicity of these antineutrophil cytoplasmic antibodies (ANCAs) and cellular anti-PR3 responses, however, remains unproven. The purpose of this study has been to generate and evaluate an in vivo model of cANCA-associated disease.

We successfully cloned, expressed and purified functional mouse PR3. The presence of PR3 was confirmed by Western blot and its enzymatic activity was assayed by synthetic substrate hydrolysis. Autoimmunity prone non-obese diabetic (NOD) mouse strain, which has a lower threshold for breaking self-tolerance, was used for immunization. The development of antineutrophil cytoplasmic antibodies against PR3 was followed by an ELISA, by indirect immunofluorescence microscopy and by flow cytometry. Disease progression was followed in control and immunized mice.

Immunization of NOD mice with rmPR3 resulted in breaking tolerance toward self-PR3 and in high levels of circulating and cell-bound PR3-ANCAs. These PR3-immunized NOD mice did not develop any apparent signs of autoimmunity despite high titers of autoantibodies. The adoptive transfer of splenocytes from PR3-immunized NOD mice into immunodeficient NOD-SCID mice resulted in the reconstitution of an immune system and the appearance of PR3-ANCAs. In striking contrast to NOD mice that had high titers of PR3-ANCA autoantibodies, the appearance of PR3-ANCAs in NOD-SCID mice resulted with kidney failure and death in the secondary recipients of splenocytes from rPR-3 immunized hosts.

Immunization of mice with mPR3 resulted with in breaking the tolerance toward self-PR3 and inducing potent anti-self PR3 immune responses. Our hypothesis is that cANCAs actively mediate glomerular injury; however, synergistic interaction between an anti-PR3 immune response and pro-inflammatory stimuli is required to induce active disease.

RISK FACTORS PREDICTING FIRST HOSPITALIZATION OR DEATH AFTER INITIATING RENAL REPLACEMENT THERAPY

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Background. The proportion of Medicare expenditures for the ESRD program has steadily grown since its inception in 1973, in 2003 accounting for 6.6%, or $18.1 billion. The ESRD program has received much attention under growing pressure to contain health care costs in the United States. Determining predictors of first hospitalization or death after initiating RRT can help identify interventions in the pre-ESRD period and potentially reduce both mortality and hospitalization costs.

Methods. A cross-sectional study of prevalent and incident adult ESRD patients in the United States Renal Database System (USRDS) between the years of 1995 and 2003 was performed (n=662,350). A Kaplan-Meier survival curve was used to model time to the combined outcome measure of first hospitalization or death from first dialysis treatment. Cox proportional hazards models were used to determine the relationship between time to the combined outcome measure and a set of risk factors.

Results. A total of 550,444 (83%) patients were hospitalized or died during the study period. Increased risk of hospitalization or death after initiation of renal replacement therapy (RRT) was independently associated with GFR > 5.7, diabetes, cardiac disease, stroke, cancer, COPD, Medicaid coverage and lack of insurance coverage. Decreased risk of hospitalization or death after initiation of RRT was independently associated with every level of hemoglobin compared to a baseline of 10.9 to 12.6 and all races compared with Caucasian race.

Conclusion. Further study can help identify the most productive pre-ESRD interventions based on epidemiologic factors and comorbidities that increase the risk of first hospitalization or death.

PROSPECTIVE QUALITY OF LIFE EVALUATION IN PATIENTS UNDERGOING TREATMENT OF RENAL CELL CARCINOMA: INTERIM ANALYSIS

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Treatment options for localized renal cell carcinoma (RCC) have rapidly expanded in the past 10 years to include laparoscopic surgery, nephron-sparing surgery (NSS), and watchful waiting (WW). We present the interim results of a prospective quality of life (QOL) evaluation in patients undergoing various forms of treatment for RCC.

Patients undergoing laparoscopic, open, radical, and NSS renal procedures, or who were undergoing WW for a renal mass were enrolled in an IRB-approved study assessing QOL using several measures. Questionnaires were administered at multiple time points.

A total of 218 patients have been enrolled to date on 3 IRB-approved protocols. Physical component scores (PCS) were different between patients undergoing laparoscopic (N=29) and open (N=24) surgery at the 1 month time point ($p=0.01$), with laparoscopy patients having higher scores, but were not significant for the other time points. Mental component scores (MCS) were also significantly different between laparoscopic and open groups at 1 month ($p=0.015$), with open surgery having higher scores. No PCS or MCS were significantly different between patients undergoing radical (N=20) versus NSS (N=33) at any time point. When evaluating the baseline QOL of patients undergoing surgery versus WW, those undergoing surgery had greater distress from intrusive thoughts and behaviors ($p=0.002$) and avoidance ($p<0.001$).

At this interim, laparoscopy seems to be associated with better short-term PCS, while short-term MCS favored patients undergoing open surgery. Patients undergoing watchful waiting of a small renal mass seem to be less distressed by their diagnosis. We suspect, however, that these popular instruments do not have enough sensitivity to measure relevant QOL outcomes in a patient population in whom renal reserve, the threat of dialysis, pain, and cancer recurrence or progression may be significant components that are unmeasured. A validated questionnaire specifically designed to evaluate the QOL of patients undergoing treatment for localized RCC is needed, and is currently being developed as part of a fourth protocol at our institution.

TRPC1 CHANNEL IS INVOLVED IN CONTRACTILE FUNCTION OF GLOMERULAR MESANGIAL CELLS

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Contractility of glomerular mesangial cells (MCs) is tightly controlled by intracellular Ca^{2+} concentration ($[Ca^{2+}]_i$). Ca^{2+} influx across the plasma membrane constitutes a major component of mesangial responses to vasoconstrictors. TRPC1 is a Ca^{2+} permeable cation channel in a variety of cell types. The present study was performed to investigate whether TRPC1 takes part in vasoconstrictor-induced mesangial contraction by mediating Ca^{2+} entry. We found that angiotensin II (Ang II) evoked remarkable contraction of the cultured MCs. Downregulation of TRPC1 using RNAi significantly attenuated the contractile response. Infusion of Ang II in rats caused a decrease in glomerular filtration rate (GFR). The GFR decline was significantly reduced by infusion of the TRPC1 antibody that targets an extracelullar domain in the pore region of TRPC1 channel. However, the treatment of the TRPC1 antibody did not affect the Ang II-induced vasopressing effect. Electrophysiological experiments revealed that functional or biological inhibition of TRPC1 significantly depressed Ang II-induced channel activation. Fura-2 fluorescence-indicated Ca^{2+} entry in response to Ang II stimulation was also dramatically inhibited by the TRPC1 antibody and TRPC1 specific RNAi. These results suggest that TRPC1 plays an important role in controlling contractile function of MCs. Mediation of Ca^{2+} entry might be the underlying mechanism for the TRPC1-associated MC contraction.

DISRUPTION OF *ROBO2* IS ASSOCIATED WITH URINARY TRACT ANOMALIES AND CONFERS RISK OF VESICOURETERAL REFLUX

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Congenital anomalies of the kidney and urinary tract (CAKUT) include vesicoureteral reflux (VUR). VUR is a complex, genetically heterogeneous developmental disorder characterized by the retrograde flow of urine from the bladder into the ureter and is associated with reflux nephropathy, the cause of 15% of end-stage renal disease in children and young adults. Despite ~1% incidence of VUR in the pediatric population, the genetic basis of VUR remains unclear. We investigated a male with a *de novo* translocation, 46,X,t(Y;3)(p11;p12)dn, who exhibits multiple congenital abnormalities including severe bilateral VUR with uretero-vesical junction defects. Using fluorescence *in situ* hybridization, we found this translocation disrupts *ROBO2*, encoding a transmembrane receptor for SLIT ligand, and produces dominant negative ROBO2 proteins that abrogate SLIT-ROBO signaling *in vitro*. By DNA sequencing, we identified two novel *ROBO2* intracellular missense mutations that segregate with CAKUT and VUR in two unrelated families. In addition, we studied a *Robo2* conditional knockout mouse, $Robo2^{flox/flox}$, and generated $Robo2^{del5/+}$ mice that lack exon 5 by crossing $Robo2^{flox/flox}$ mice with the $Tg^{EIIa\text{-}Cre}$ deletor strain. $Robo2^{del5/del5}$ homozygotes uniformly died shortly after birth with multiplex, dysplastic kidneys and atrophic ureters. While $Robo2^{del5/+}$ heterozygotes were viable, adult heterozygous and mosaic mutant mice with reduced *Robo2* gene dosage also exhibit striking CAKUT-VUR phenotypes. Collectively, these results implicate the SLIT-ROBO signaling pathway in the pathogenesis of a subset of human VUR.

HSP27, A PRO-SURVIAL FACTOR, INHIBITS BAX ACTIVATION & APOPTOSIS VIA AN AKT-DEPENDENT MECHANISM

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Renal ischemia *in vivo* and exposure to metabolic inhibitors *in vitro* cause mitochondrial membrane injury associated with bax activation and apoptosis in proximal tubule epithelial. Hsp27, an inducible heat stress protein, reduces apoptosis in diverse cells types by an unknown mechanism. To evaluate the hypothesis that hsp27 inhibits Bax activation and apoptosis, renal epithelial cells (REC) were infected with adenovirus (AdV) containing human hsp27 prior to pharmacologic ischemia, an insult that activates bax and induces apoptosis. Hsp27 over-expression inhibited bax activation detected by a conformation specific antibody, reduced mitochondrial leakage of both cytochrome c and apoptosis inducing factor (AIF) and improved survival by >50% after 1-2 hr pharmacologic ischemia compared to empty vector. Immunoprecipitation (IP) did not detect hsp27-bax interaction before, during or after ischemia, suggesting that hsp27 does not directly regulate bax. To determine whether hsp27 indirectly antagonizes bax via Akt, a pro-survival serine-threonine kinase that phosphorylates and inactivates bax, p-ser^{473}Akt (active) and total Akt content were compared at baseline and after ischemia in hsp27 over-expressing and in control cells. Hsp27 over-expression increased p-Akt content both at baseline and after ischemia compared to empty vector without altering total Akt. Hsp27 over-expression and ischemia selectively increased the interaction between hsp27 and Akt detected by IP. Hsp27 over-expression did not appear to alter the apparent half-life of p-ser^{473}Akt during metabolic stress, an insult, which inactivates Akt, suggesting that hsp27 does not inhibit PP2-mediated Akt dephosphorylation. Ly294002 and wortmannin (two distinct Akt/PI3 kinase inhibitors) completely abrogated the pro-survival effect of hsp27, showing that Akt activation and bax inactivation are central to improved REC survival after injury. These data support the hypothesis that hsp27 indirectly inhibits bax-mediated mitochondrial injury and apoptosis after in vitro ischemia by facilitating Akt activation via a PI3 kinase-dependent pathway. Both Akt and hsp27 represent potential new targets for improving REC survival after an ischemic insult.

NAD(P)H OXIDASE NOX4 IS A NOVEL SOURCE OF REACTIVE OXYGEN SPECIES IN THE MITOCHONDRIA.

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Oxidative stress has been implicated in diverse human diseases including diabetes and atherosclerosis as well as in aging. The bulk of oxidative pathways are harbored in the mitochondria, where various redox carriers leak electrons to oxygen to form superoxide anion. In phagocytic cells, however, $gp91^{phox}$-based NAD(P)H oxidase has long been recognized as a major source of reactive oxygen species (ROS). More recently, several isoforms of $gp91^{phox}$, called Nox proteins, have been cloned and identified in somatic cells. Nox4 was cloned from the kidney and we have recently shown that it is a major source of ROS in renal cells and kidney tissue of diabetic animals. We generated specific rabbit polyclonal Nox4 antibodies and found that Nox4 localizes to mitochondria. Several approaches were utilized to confirm Nox4 localization. (i) Immunoblot analysis in cultured rat glomerular mesangial cells (MCs) as well as renal cortex revealed that Nox4 was present in crude mitochondrial fractions, in mitochondria-enriched heavy fractions and in purified mitochondria. (ii) Independent confirmation of Nox4 localization to the mitochondria was analyzed by immunogold electron microscopy. (iii) Immunofluorescence confocal microscopy was also used to localize Nox4 in MCs. Our observation was confirmed using the mitochondrial localization prediction program MitoProt, where the probability score for Nox4 obtained was identical to mitochondrial protein human cytochrome c oxidase subunit IV. Functionally, siRNA-mediated knockdown of Nox4 reduces NADPH oxidase activity in pure mitochondria and blocks glucose-induced mitochondrial superoxide generation. Our data provide the first evidence that a functional Nox4 is present and regulated in mitochondria, indicating the existence of a novel source of ROS in this organelle. Our findings offer a possible explanation for the data of the literature reporting that both mitochondria and Nox-containing oxidases are sources of ROS. The present demonstration that Nox4 resides in mitochondria and plays a key role in disease-induced oxidative stress may reconcile the mitochondrial and the NAD(P)H oxidase hypotheses.

PERMANENT EXPOSURE OF A CRYPTIC ACTIN BINDING SITE IN FSGS-CAUSING MUTANT ALPHA-ACTININ-4

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We have identified 5 mutations in the head domain of the actin crosslinking protein -actinin-4 which cause an autosomal-dominant and slowly progressive form of focal segmental glomerulosclerosis (FSGS).

All mutations lead to increased actin binding and form large cytoplasmic aggregates in cultured cells. These aggregates occur in podocytes *in vivo*, are highly insoluble and contain large amounts of actin, suggesting that glomerular damage in this disease is caused by a direct effect on the podocyte actin cytoskeleton. By means of *in vitro* studies, we further defined the effect of one disease-causing mutation (K255E) on actin crosslinking. Using recombinant proteins, mutant -actinin-4 shows dramatically increased actin binding affinity, resulting in the formation of a greatly altered actin filament network structure with different viscoelastic properties. Furthermore, the stochiometry of -actinin-4/actin molecules was increased. Supported by recent data on the crystal structure of -actinin-1, we postulated that an otherwise buried actin binding site is exposed or activated by the mutation. In further experiments, inactivation of this buried actin binding site by site-directed mutagenesis returned the actin binding affinity of the mutant to that of the wild type protein but showed no effect on wild type -actinin-4.

We propose that the mutation locks the head domain of -actinin-4 in one conformation, thereby exposing a high-affinity actin binding site which leads to dysregulation of the actin binding properties of -actinin-4. Over time, this results in direct structural damage of the actin cytoskeleton in the podocyte foot process and ultimately foot process effacement with destruction of the glomerular filter.